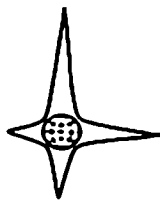


K. BUNIN

**INFECTIOUS
DISEASES**

A TEXTBOOK FOR SECONDARY MEDICAL SCHOOLS

MIR PUBLISHERS • MOSCOW



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Инфекционные болезни

Учебник для учащихся медицинских училищ

ИЗДАТЕЛЬСТВО «МЕДИЦИНА» МОСКВА

На английском языке

Professor K. Bunin

INFECTIOUS DISEASES

A TEXTBOOK FOR SECONDARY MEDICAL SCHOOLS

**Translated from the Russian
by
David A. Myshne**

MIR PUBLISHERS • MOSCOW

Contents

Foreword	9
Introduction	11

General Information

History of Theories of Infectious Diseases	15
General Pathology of Infectious Diseases	26
Classification of Infectious Diseases	38
Principal Methods of Diagnosing Infectious Diseases	42
Organization of and Regimen in Contagious Hospitals and Departments	49
Purpose of Contagious Hospitals (Departments)	49
General Organization and Lay-Out of Contagious Hospitals (Departments)	49
Work of the Admission Department	51
Work of a Contagious Department	55
Rules Governing the Work of the Personnel of Contagious Departments	59
Prevention of Nosocomial (Intrahospital) Infections	59
Care and Diet of Infectious Patients	61
Principal Methods of Treating Infectious Patients	66
Disinfection, Disinsection and Deratization	77
Fundamentals of Infectious Disease Prevention	78

Clinical Information

I. INTESTINAL INFECTIONS	91
Typhoid Fever	91
Paratyphoid Fever A and Paratyphoid Fever B	108
Food Poisoning	110
Botulism	115
Dysentery	120
Amoebiasis	132
Asiatic Cholera	138
Botkin's Disease	145
Helminthiases	158

II. TRANSMISSIVE (BLOOD) INFECTIONS

Classic Epidemic (Louse-Borne) Typhus	
Tick-Borne Typhus or North-Asian Ixodorickettsiosis	
Endemic or Murine Rickettsiosis	
Q Fever	
Relapsing Fever	
Tick-Borne Relapsing Fever	
Malaria	
Cutaneous Leishmaniasis	
Visceral (General) Leishmaniasis	
Pappataci Fever	
Haemorrhagic Fevers	
Epidemic Encephalitides	
Seasonal Encephalitides	
1. Tick-Borne Spring-Summer (or Taiga) Encephalitis	
2. Mosquito-Borne Summer-Autumn (Japanese) Encephalitis	

III. ZOONOTIC INFECTIONS

Rabies	
Brucellosis	
Icterohaemorrhagic Leptospirosis or Weil-Vasilyev's Disease	
Marsh Fever or Anicteric Leptospirosis	
Glanders	
Anthrax	
Tularaemia	
Plague	
Foot-and-Mouth Disease	

IV. AIR-BORNE (DROPLET) INFECTIONS

Chickenpox	
Influenza	
Diphtheria	
Infections Mononucleosis	
Whooping Cough	
Measles	
Rubella (Morbilli)	
Fetharizic Encephalitis (Economo's Disease)	
Smallpox	
Ornithosis	
Acute Anterior Poliomyelitis	
Scarlet Fever	
Epidemic Cerebrospinal Meningitis	
Mumps (Epidemic Parotitis)	

V. INTEGUMENTARY INFECTIONS

Erysipelas	
Tetanus	
Complications of Drug Therapy and Methods of Preventing Them	

Supplements

<i>Supplement 1.</i>	Incubation Periods of Various Infectious Diseases. . .	429
<i>Supplement 2.</i>	Methods of Taking Material for Laboratory Examination	431
<i>Supplement 3.</i>	M. A. Morozov's Method of Silvering for Viroscopy .	437
<i>Supplement 4.</i>	Staining Smears and Thick Drops for the Purpose of Revealing Malarial Plasmodia and Relapsing Fever Spirochaetes	437
<i>Supplement 5.</i>	Liver Function Tests in Botkin's Disease	439
<i>Supplement 6.</i>	Rules Governing Discharge of Convalescents from Hos- pital after Treatment with Drugs and Antibiotics . .	439
<i>Supplement 7.</i>	Prescriptions	441

Foreword

The first edition of the textbook was given a positive appraisal in the periodic press and in discussions by numerous teaching staffs of secondary medical schools.

In preparing this edition the author took into account the critical remarks made by reviewers.

The author deemed it necessary to include in this textbook the latest scientific information and results of the practical achievements of Soviet medicine. The author extended those parts of the textbook in which science has lately become enriched with new facts which are of particular practical value. The parts of the textbook dealing with methods of diagnosing infectious diseases, the principles of their treatment with antibiotics were written anew. The book also contains new descriptions of the complications of drug therapy, use of therapeutic serums, and a new chapter on Economo's lethargic encephalitis.

New illustrations have been added and the old ones improved; the book also contains a number of original, including coloured, pictures and photographs.

In view of the existence of a special textbook on disinfection the author found it possible to limit himself to the most essential information on this subject, thereby shortening the corresponding chapter compared with the first edition of the textbook. The parts of the textbook printed in small type are aimed at giving the students deeper insight into the material.

To help the students to master the materials presented in the textbook, the latter includes tables of differential diagnostic signs of the main types of diseases. The supplements contain information which is of practical interest.

The author hopes that the present edition of the textbook will be helpful to the students and will be favourably received by teachers.

Author

Among the various human diseases a special part is played by diseases caused by pathogenic microorganisms and transmitted to healthy people from sick people or animals.

These diseases are particularly characterized by their ability to affect masses of people owing to development of epidemics. In the 19th century these diseases were given the general name of *infectious diseases* (from the Latin *inficere*—to infect).

Infectious diseases brought great misfortune to the people of different countries even in remote historical epochs; in times of war, famine and natural calamities infectious diseases repeatedly developed into epidemics.

Medieval and modern history, as well as the history of our own days, has known quite a number of devastating epidemics of such severe infectious diseases as the plague, smallpox, typhus and cholera.

The development of scientific knowledge concerning the nature of infectious diseases, the rise in the cultural standards of the population and the improved sanitation and hygiene in a number of civilized countries greatly contributed to the successful control of infectious diseases already at the end of last century.

The plague, cholera, smallpox and relapsing fever have long since been eradicated in the USSR; malaria has also been practically stamped out.

Considerable efforts in the struggle against infectious diseases are also being made in member-countries of the World Health Organization. In 1955, the World Health Assembly launched a systematic international campaign against malaria. Practice has shown that enormous results may be achieved on this basis; the experience obtained in the control of malaria on Crete and Sardinia has convincingly demonstrated the importance of complex antimalarial drugs. The basic measures used in the control of malaria include disinfection of human dwellings with insecticides, which is aimed at exterminating the carrier of malaria—the *Anopheles* mosquito, individual and community chemoprophylaxis of malaria, revealment of malaria patients and their rational treat-

ment with the most effective drugs, and prevention and treatment of relapses of the disease; these measures make it possible to eradicate the disease even where the incidence of this disease was formerly very high.

In out-of-the-way places and communities scattered over a vast territory antimalarial drugs are added to the common salt. The results of the struggle against malaria in a number of WHO member-countries indicate that it is now possible completely to eradicate malaria all over the world.

However, control of malaria is not the only urgent problem. The important health problems to be solved in the nearest future include eradication of poliomyelitis, rabies and tularaemia; it is also necessary to reduce the incidence of typhoid fever, brucellosis and a number of other infectious diseases. These aims can be achieved in different countries by steadily improving the material and cultural standards of the population, adopting extensive sanitary and hygienic measures, planning the work of the health services and utilizing the latest achievements of science. That these aims can be attained is convincingly attested by the experience of the Soviet Union.

The WHO is also devoting considerable attention to immunization in order to prevent a number of infectious diseases; the measures of immunization include inoculations against smallpox, tetanus, whooping cough, diphtheria and poliomyelitis.

To succeed in the struggle against infectious diseases, medical workers must be given good training in the clinical aspects, diagnosis and treatment of these diseases. The present textbook is aimed at helping the students to acquire solid theoretical knowledge of infectious pathology.

General Information

HISTORY OF THEORIES OF INFECTIOUS DISEASES

The first theories of infectious diseases originated in antiquity. The ideas that such diseases as the plague, smallpox, cholera, etc., are communicable occurred already to the ancients; this is attested by the fact that certain very simple measures of precaution with regard to contagious patients were adopted long before the Christian era. However, the fragmentary observations and bold conjectures of the ancients were far from true scientific knowledge.

Certain ancient Greek philosophers, for example, Thucydides, suggested that infectious diseases were caused by living agents ("contagions"), but were unable to confirm their suppositions by any authentic facts.

Hippocrates (about 460-377 B.C.), outstanding physician of the ancient world, explained the origin of epidemics by the action of "miasmas"—noxious emanations which were allegedly capable of causing a number of diseases.

Even under the conditions of medieval scholasticism the progressive minds correctly suggested that the causative agents of contagious diseases were living organisms. For example, the Italian physician Girolamo Fracastoro (1483-1553) developed a harmonious theory concerning contagious diseases and the methods of their transmission in his classical work *On Contagions and Contagious Diseases* (1546).

The Dutch naturalist Anton van Leeuwenhoek (1632-1723), made a very important discovery at the end of the 17th century; under the microscope (which he had personally constructed and which multiplied images 160-fold) he found various microorganisms in tartar, in stagnant water and in plant decoctions. He thus discovered the invisible-to-the-naked-eye world of microbes, many of which could apparently have been causative agents of diseases. He described his observations in the book *Secrets of Nature Discovered by Anton Leeuwenhoek*. But even after this discovery the idea about microbes as causative agents of infectious diseases long failed to be substantiated scientifically, although devastating epidemics repeatedly occurred in various countries of Europe and took a toll of thousands of human lives.



A. Leeuwenhoek

For many many decades (in the 17th and 18th centuries) observations of epidemics of infectious diseases which affected large numbers of people indicated that these diseases were *contagious*.

The works of the English scientist Edward Jenner (1749-1823), who elaborated a highly effective method of inoculations against cowpox, proved to be of particular practical importance.

The contemporary Russian epidemiologist D. S. Samoilovich (1841-1914) showed that the plague was contagious when a healthy person was brought into contact with a patient; he also elaborated effective methods of disinfection for this disease. However, the causative agent of the disease was for the first time isolated in the 1890's.

Microbiology began with the French scientist Louis Pasteur (1822-1895), who experimentally demonstrated the role of microorganisms in processes of fermentation, putrefaction and in the development of infections. He also worked out methods of preventing beer and wine from becoming sour for the brewing and distilling industries.

Pasteur's work explained the real origin of man's infectious diseases and served as the experimental basis of asepsis and anti-



E. Jenner

sepsis brilliantly elaborated in surgery by N. I. Pirogov, Joseph Lister and their numerous followers and pupils. Pasteur's enormous contribution to science was his discovery of the principle of producing *vaccines* for preventive inoculations against infectious diseases, namely, attenuation of the virulent properties of causative agents by choosing appropriate conditions for their cultivation. Pasteur developed vaccines for anthrax and rabies. Pasteur's great contributions will live forever in the history of world science.

Several causative agents of infectious diseases were discovered in the second half of the last century; they included those of relapsing fever (1873), anthrax (1876), typhoid fever (1880), tuberculosis (1882), glanders (1882), plague (1894) and a number of other diseases.

Robert Koch (1843-1910), outstanding German microbiologist, not only described the morphological characteristics of the causative agents of cholera and anthrax but also provided physicians with methods of staining bacteria with aniline dyes and of producing pure cultures of *pathogenic* microbes in dense nutrient media.

The progress of scientific knowledge in the aetiology of infectious diseases was fostered by the discovery of *protozoa* as causative agents of various infectious diseases (amoebiasis—1875, malaria -1880,



L. Pasteur

and in 1878. The important studies of D. I. Ivanovsky proved the existence of minute microorganisms—filtrables—which go through the pores of a bacterial filter.

German scientist Friedrich A. J. Loeffler proved in 1897 that foot and mouth disease is caused by a filtrable virus.

It should be noted that until the very middle of the last century infectious diseases known as "fevers" were never differentiated. In 1813 did the French physician Pierre Bretonneau voice the assumption that typhoid fever was a distinct disease entity.

Pierre Louis gave a detailed description of the clinical picture of this disease in 1829.

In 1856 typhoid fever and typhus were separated from the group "febrile diseases" and were clearly described as distinct diseases. Relapsing fever also began to be recognized as a distinct infectious disease in 1865. All these diseases were given complete clinical description in the clinical lectures of the outstanding internists S. P. Botkin and A. A. Ostroumov.

P. Vassiliev (1852-1894), noted Russian infectious-disease specialist, set apart the so-called infectious jaundice (icterohaemor-



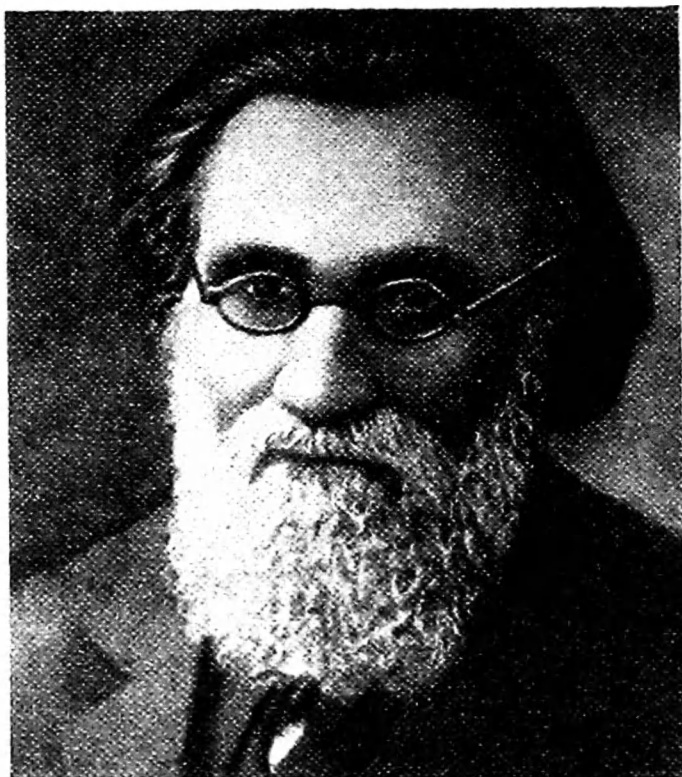
R. Koch

rhagic leptospirosis) as a distinct nosological entity, and demonstrated that the same causative agent produced glanders in man and animals.

World science has properly appraised the works of the well-known Russian clinical pediatricist N. F. Filatov (1847-1902), who made an important contribution to the study of children's infectious diseases, and D. K. Zabolotny (1866-1929), who conducted a number of important observations in the epidemiology of especially dangerous diseases (plague, cholera). Many questions of infection and immunity found reflection in the works of N. F. Gamaleya (1859-1949).

The important clinical sign of the early stage of measles --bran-like scaling of the oral mucosa--was discovered by the Pskov physician A. P. Belsky in 1890 and, independently of him, by N. F. Filatov in 1895.

Pathoanatomical studies, which in a number of infectious diseases discovered characteristic changes manifested in the presence of specific cellular nodules in the tissues (granulomas), for example, in patients who had died of typhus (1875), tuberculosis (1883)



I. I. Mechnikov

and glanders (1886), made a considerable contribution to the correct understanding of pathogenesis, i.e., the origin and development of infectious diseases.

The contributions made by L. V. Popov should be particularly emphasized; he was the first to describe infectious granuloma, i.e., perivascular nodules in the brain of people who had died of typhus.

Medical microbiology began its rapid development in the second half of the 19th century. In the beginning of the 20th century we already had clear scientific ideas about the aetiology, mechanisms of infection and routes of transmission of a number of infectious diseases, and were in a position to carry out a number of hygienic measures aimed at preventing these diseases.

The great Russian physiologist I. P. Pavlov (1849-1936) fervently hailed the brilliant achievements of microbiology made at the end of the last and the beginning of the current centuries, believing that this then as yet young science was destined to make many new discoveries in the field of human pathology.

The works of I. I. Mechnikov (1845-1916) and a number of other researchers started contributing in the 1880's to the solution of



S. P. Botkin

problems of immunity (insusceptibility) to infectious diseases, and showed the exceptionally important role played by cellular (phagocytosis) and humoral (antibodies) defences of the organism. An important contribution to the research in immunity was made by such prominent scientists as V. K. Vysokovich, J. J. Bordet, and others.

In addition to purely clinical examinations of infectious patients, laboratory methods of diagnosing various diseases began to be widely used at the end of the 19th century.

The investigations conducted by a number of scientists (I. I. Mechnikov, V. I. Isayev, F. Y. Chistovich, G. F. Widal, P. Uhlenhuth) made it possible as early as the end of the last century to utilize serological tests (agglutination, lysis and precipitation) for laboratory diagnosis of infectious diseases.

In 1896 G. Widal proposed (in France) an agglutination test for diagnosing typhoid fever.

Two Russian scientists—H. I. Gelman and O. Kalning elaborated a method of allergic diagnosis of glanders (1892). The diagno-



N. P. Vasilyev

st. of malaria was considerably facilitated by the method of differential staining of the nucleus and protoplasm of the malarial plasmodium in blood smears developed by D. L. Romanovsky (1892).

The studies in pathology and epidemiology of infectious diseases were considerably facilitated by investigations of experimental infections of animals.

Long before the appearance of L. Pasteur's outstanding studies which elucidated the role of microbes in human pathology S. S. Andreyevsky (1786) had demonstrated by a selfless experiment (he inoculated himself with the contents of an anthrax carbuncle of a diseased animal) that the same agent causes anthrax in man and domestic animals.

In the 1870's to prove that the infectious agent of typhus and relapsing fever is present in the patient's blood, O. O. Mochutkovsky and G. N. Minkh, physicians of an Odessa city hospital, injected under their own skin the blood of patients and thereby contracted this very severe disease.

Questions of experimental infections were fruitfully studied also



E. N. Pavlovsky

by other scientists. For example, F. A. Lesh reproduced amoebiasis in dogs in 1875. I. I. Mechnikov obtained a number of important scientific data by experimentally reproducing relapsing fever in monkeys and anthrax in pigeons.

After the victory of the Great October Socialist Revolution control of infectious diseases was undertaken on a very wide scale. An important part in the studies of the epidemiology of a number of infectious diseases was played by research of Soviet scientists, especially that of Academician E. N. Pavlovsky (1884-1965) who has shown that such infectious diseases as the plague, leishmaniasis, seasonal encephalitides, pappataci or phlebotomus fever, etc., have *natural foci*.

Specific methods of preventing infectious diseases have been successfully elaborated in the USSR over a number of years; living vaccines for tularaemia, brucellosis, anthrax, plague, smallpox and certain other infectious diseases are now used with good results.

Elaboration of methods of active treatment of infectious diseases constitutes an important part of the theory of these diseases. A decoction of cinchona bark has long been successfully used in the

treatment of malaria patients; quinine, an alkaloid, the first of the chemotherapeutic agents obtained synthetically has been used since 1821. Quinine is widely utilized in the prevention and treatment of malaria. However, the development of chemotherapy was impeded for a long time. Only in 1909 did arsenicals (first arsacetin and then salvarsan [arsphenamine], neosalvarsan, etc.) appear in medical practice; these arsenicals synthesized in Germany were later successfully used in the treatment of relapsing fever, syphilis, anthrax and certain other infectious diseases.

Antimony preparations began to be used for the treatment of visceral leishmaniasis somewhat later, these preparations proved very effective. Synthetic preparations of sulpha drugs (streptocide, sulphidine [sulphapyridine], sulphazole [sulphamethylthiazole], etc.) were produced in the 1930's and were followed by antibiotics (penicillin—1941, streptomycin—1944, chloromycetin [chloramphenicol], and their analogues—1948, and later—biomycin [chlorotetracycline], terramycin, albomycin, tetracycline, colimycin, mycerin, bicillin, nystatine, etc.).

In 1871 the noted Russian scientist V. A. Manassein and later A. G. Polotebnov observed the *Penicillium glaucum* to exert an antagonistic influence on certain bacteria. Polotebnov also used the *Penicillium glaucum* for the treatment of gummous ulcers and purulent wounds.

An uncommonly important contribution was made by the observations of the English microbiologist Alexander Fleming who discovered in 1929 that broth filtrates of the *Penicillium notatum* possess the ability to retard the growth of the staphylococcus and of a number of other gram-positive bacteria.

On the basis of the foregoing facts Howard W. Florey elaborated a complex technology of isolating active substances from the aforementioned molds and produced the antibiotic penicillin in 1941.

Soon afterwards penicillin and a number of other antibiotics began to be widely used in medical practice. Today antibiotics play the most important part in the treatment of a number of infectious diseases; the search for new antibiotics and their clinical tests continue apace.

The successful use of chemotherapeutic preparations and antibiotics in various infectious diseases opened enormous prospects in controlling these severe diseases.

Chemical prevention of malaria by means of daily administration of small doses of quinine (0.15-0.25 g per day) to persons who were in danger of contracting the disease was first carried out by the Russian army physician A. Yassinsky (1858); later, the same principle of preventing malaria chemically was successfully used by M. I. Manotskov in Turkestan, and by Robert Koch, noted German scientist, abroad.

The studies conducted by E. Behring in Germany and Pierre



A. Fleming

Roux in France led to the use of antitoxic and antibacterial *serums* in certain infectious diseases in the 1890's. Such serums were first used in the treatment of diphtheria; later, a number of serums were produced and successfully employed in the treatment of botulism, anthrax, etc. Today immune gamma globulins are effectively administered in a number of infectious diseases; these agents have in large measure replaced serums.

Progressive scientists the world over have always directed their efforts towards controlling infectious diseases.

By the end of the 19th century the specific features of infectious diseases necessitated the teaching of a corresponding independent discipline. The first faculty of infectious diseases was established in Russia in 1896; it was headed by Associate Professor S. S. Botkin (son of the noted internist S. P. Botkin) and after 1898 by F. Y. Chistovich.

Until 1923 the course in infectious diseases in universities was taught by professors of departments of internal diseases; practical studies were conducted in the same departments. In 1923 a department of infectious diseases with Professor M. P. Kreyev at its head was established in the Medical Faculty of Moscow University (today

the First Moscow Sechenov, Order of Lenin, Medical Institute). Later, departments of infectious diseases were organized in all other medical faculties and medical institutes. The specialists in infectious diseases—N. K. Rosenberg (1876-1933), G. A. Ivashentsov (1883-1933), and others were not only brilliant teachers and clinicians; they also enriched science with important investigations in various branches of infectious pathology. Today Soviet scientists are successfully working on problems dealing with active control of infectious diseases.

Courses in infectious diseases are taught in all Soviet medical institutes and secondary medical schools. The entire system of training medical specialists must ensure successful studies of various infectious diseases. Every medical student must master the theory and practice of controlling infectious diseases and must aim at consolidating the achievements of preventive medicine.

GENERAL PATHOLOGY OF INFECTIOUS DISEASES

The most important characteristic of infectious diseases is that they are caused by harmful (pathogenic) microorganisms. However, this factor alone is not enough; for an infectious disease to develop, the human (or animal) organism must be susceptible to the given infection and must respond to the invasion of the particular microbe by a complex pathophysiologic and morphologic reaction which determines the clinical picture and all other manifestations of the disease.

Infectious diseases are characterized by a definite aetiology (pathogenic microbe or its toxins), not infrequently by a tendency for extensive epidemic spread, communicability, cyclic nature of their course, formation of immunity, and, in particular, their chronic forms or possible development of germ-carrying.

As a rule, every infectious disease has its own *specific causative agent*. For example, typhoid fever is caused by typhoid fever bacteria, typhus - by *Rickettsia prowazeki*. Only in comparatively rare cases do two or more infectious diseases with different causative agents happen to have very similar clinical pictures (for example, typhoid fever, paratyphoid A and paratyphoid B). Still less frequently does an infectious disease prove to be polyaetiological (for example, sepsis), i.e., the causative agents of the disease may be various microbes, but in these cases, too, it is possible to observe a number of peculiarities in the clinical picture associated with the *virulence* and *other properties* of the causative agents (p. 30).

The role of a causative agent of an infectious disease may be played by various pathogenic microorganisms; *bacteria* (their main types are shown in Fig. 1) cause diphtheria, typhoid fever, leptospirosis, etc.; *rickettsiae* produce typhus; *filtrable viruses* provoke measles



Fig. 1. Most important forms of bacteria
1-6—cocci; 7-9—bacilli; 10—vibrios; 11—spirilla; 12—spirochaetes

and Botkin's disease; *protozoa* are responsible for amoebiasis; *fungi* cause actinomycosis.

The numerous investigations in the morphology of filtrable viruses conducted in recent years by means of the electron microscope (Fig. 2) have considerably extended the scientific knowledge about these causative agents of infectious diseases.

The effect produced by an infectious agent on the human organism is due to the ability of the microbial cell to invade the organism.

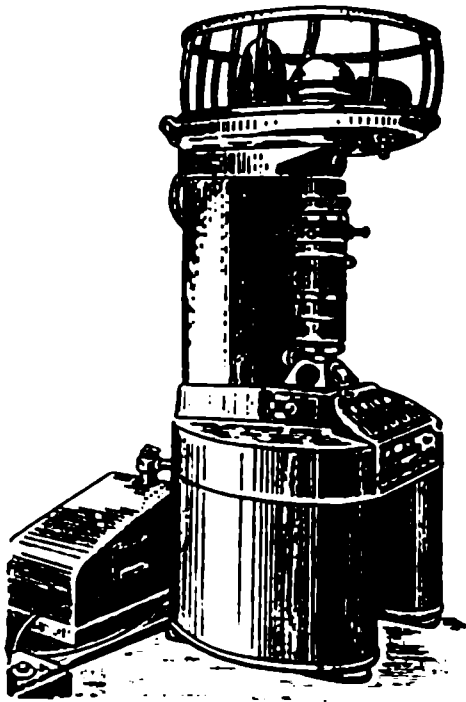


Fig. 2. Electron microscope

its mobility and also due to endo- and exotoxins of the microbe. The pathologic phenomena associated with the action of microbial exotoxins on the organism dominate in the clinical picture of many infectious diseases (diphtheria, botulism, tetanus, gas gangrene).

The response reactions of the organism to the invading pathogenic microbe or to the action of the exotoxin involves all physiological systems regulated as a single whole by the nervous system and corrected by specific

humoral and endocrine products formed in the organism.

Moreover, specific *cell reactions* take place in many infectious diseases (as is the case in the development of general vasculitis in typhus patients) and the chemism of the tissues is altered, which in addition to the production of *antibodies* forms the general system of defence and adaptation mechanisms. An important part in this is played by reactions of the mesenchyme and production of antibodies by the plasma cells.

The course and results of infectious diseases depend on the preceding physiologic state of the most important organs and systems (nervous, cardiovascular, respiratory, etc.). For example, the presence of previous disturbances in intestinal activity may contribute to production of chronic dysentery. The clinical picture of infectious diseases is substantially affected by inoculations (for example, mitigated measles in patients inoculated with gamma-globulin).

In patients malnourished *before* the development of an infectious disease the reaction of the organism in the pathologic process is very often weak: the disease not infrequently runs a long or an atypical course and yields with difficulty to usual treatment (for example, bacterial dysentery).

Most infectious diseases are characterized by *cycles*, i.e., a definite succession in the development, intensification and abatement of the symptoms. These cycles are particularly clearly manifest in such diseases as measles, smallpox, typhus, etc. The cyclic course

of an infectious disease is the result of parasitism and spread of the causative agent in the organism, the result of definite response reactions of the patient's organism to the action of the particular microbe, the reactions occurring in definite succession and the concrete symptomatology which forms the clinical picture of the disease. The specificity of an infectious disease finds its expression in numerous phenomena of insusceptibility (immunity) which occur in the process of infection (formation of agglutinins, precipitins, etc.). The cyclic course of infectious diseases may be disturbed by development of most acute pathologic states (for example, circulatory collapse, haemorrhages into the adrenals with a resultant Waterhouse-Friederichsen syndrome), due to various complications or concurrent diseases (influenza, angina, etc.). The cyclic nature of the clinical course is clearly pronounced in such infectious diseases as smallpox and measles.

Some infectious diseases (including sepsis of various aetiology, miliary tuberculosis, meningococcaemia) develop without any definite succession in intensification and abatement of the symptoms, i.e., *acyclically*.

The following forms of infectious diseases are distinguished according to the speed of development of the clinical picture and the general course: (a) fulminating, (b) very acute, (c) acute, (d) sub-acute or protracted, and (e) chronic. Most infectious diseases are acute.

New information has been accumulated in recent years concerning the role of the nervous system in the onset, development and abatement of the infectious process accompanied by formation of some degree of insusceptibility. However, the state of this question does not as yet warrant a simple and concrete description of a theory concerning the role of the nervous system in infectious diseases, for which reason we must confine ourselves in the special part of this textbook to separate examples merely attesting this role.

Microbes may invade the human organism by devious routes--through the skin, tonsils, mucous membranes of the respiratory tract, digestive tract, etc. The site of invasion of the organism is called *the portal of entry*. In some infectious diseases the microbe may have but one portal of entry (for example, in dysentery the portal of entry is the gastrointestinal tract); in other diseases it may have several portals of entry (for example, in tularaemia--the skin, tonsils, mucous membranes of the upper respiratory tract, the gastrointestinal tract and the conjunctiva).

Whatever the action of the microbe on the organism, the response reactions of the organism in some measure involve all the physiologic systems. These reactions of the organism as a single whole are regulated by the nervous system.

The ability of a microbe to cause a pathologic process in the organism is called its *pathogenicity*. Under prolonged influences

of various conditions in the external environment the selfsame microbe may vary in its pathogenicity. The degree or extent of pathogenicity is called *virulence*.

As was already mentioned, some microbes produce poisonous substances (toxins) which are excreted from the microbial cell into the external environment. *The toxigenicity* of a microbe implies its ability to produce toxin of certain virulence. The circulation of microbial toxins in the blood (for example, in diphtheria, tetanus, botulism) is called *toxycosis*; toxycosis causes a number of disturbances in the organism.

One of the manifestations of toxycosis may be the development of *typhoid* status (Fig. 3); considerable intoxication may give rise to clouded consciousness, coma, delirium and extreme excitement.

From the site of their initial invasion microbes may spread throughout the organism; for example, in typhoid fever the causative agents of the disease circulate in the blood all through the febrile period; this condition is called *bacteraemia*.

From the patient's organism the microbes may be excreted by various routes—in the faeces, urine, sputum, etc. In addition to the main routes of excretion (for example, in the faeces through the intestines in typhoid fever), there are also collateral routes (through the urinary tract in typhoid fever).



Fig. 3. Patient with typical typhoid status

An infectious disease may end either in complete recovery or death. In some cases, however, microbes long continue to exist in the organism (bacteria-carrying) even after the end of the period of active manifestations of the disease. Lastly, a chronic disease may develop, as is the case, for example, in chronic dysentery which lasts many months and even years.

Several successive periods are distinguished in the course of an infectious disease: incubation period, prodromal period, period of active manifestations of the disease, which usually coincides with a rise in temperature, and convalescence.

The clinical picture of an infectious disease is determined by the aggregate of the general pathologic signs (rise in temperature, some measure of intoxication, headache, loss of consciousness, etc.) and characteristic dysfunction of various organs and systems. The symptomatology of infectious diseases is considered in greater detail in the chapter "Basic Methods of Diagnosing Infectious Diseases" and in the description of various nosological forms.

The period from the moment of invasion of the organism by the pathogenic microbe to the appearance of the first clinical signs of the disease is latent and is called the incubation period; during this period the causative agents multiply and spread throughout the organism, and very complex processes of reorganization of the physiologic defence mechanisms of the organism take place. This period necessarily occurs in every infectious disease. The duration of the incubation period varies widely—from several hours (botulism, toxinfection) to several weeks and even months (tetanus, rabies).

Knowledge of the duration of the incubation period of a particular infectious disease which is suspected in the patient makes it possible to compare the limits of the incubation period with the length of time which has elapsed from the moment of the possible infection to the appearance of the first clinical signs. This is very helpful in establishing a correct diagnosis.

Epidemiological data and the duration of the incubation period help to solve a number of problems concerning the establishment of quarantines, elucidation of intrahospital infections, and necessary observation of the focus of the infectious disease.

The incubation period is followed by the *prodromal* period during which the first precursors of the disease appear. Most commonly they contain nothing specific and manifest themselves in headache, indisposition, slight rise in temperature, etc. In some infectious diseases certain characteristic signs may manifest themselves already during the prodromal period; for example, during the prodromal period of measles the oral mucosa may exhibit branlike scaling (Belsky-Filatov-Koplik's sign), and during that of smallpox—skin eruptions of characteristic localization.

The prodromal period is followed by the period of *active* manifestations of the disease, i.e., the complete clinical picture of the disease.

Three stages of the active period of the disease are distinguished: the *initial* stage, *height* of the disease and the stage of *abatement* of all pathologic manifestations.

The disease is not equally contagious during its various periods; this depends on the distribution of the microbes in the organism and on the routes of their elimination. For example, a measles patient is contagious mainly during the prodromal period and in the first day of eruption; subsequently, his contagiousness sharply diminishes.

The vibrios of Asiatic cholera isolated from the patient's stool are much less virulent at the end of the disease than they are in its beginning.

As was already mentioned, most infectious diseases are characterized by *cycles*, i.e., a definite succession of the appearance, intensification and abatement of the symptoms, often in regular proportions (measles, smallpox). For example, the appearance of the tongue in scarlet fever (see Fig. 6), which is a typical sign of this disease, essentially varies with the periods of the disease.

To establish the diagnosis according to clinical signs, and to be able to isolate the causative agent in laboratory tests it is important to know the period of the disease. For example, the causative agent of typhoid fever may be isolated from the patient's blood all through the febrile period, although it is best done in the early stages of the disease. The period of a disease is very important for the purpose of prescribing an appropriate regimen and diet for the patient. This is clearly attested by typhoid fever patients who, owing to the danger of complications, must be strictly confined to bed and must be prescribed a sparing diet at the end of the third and during the fourth week of the disease. This is due to the clinical characteristics of this period of the disease—development of a deep ulcerative process in the wall of the small intestine.

Some infectious diseases—sepsis, miliary tuberculosis—are characterized by the absence of cycles.

The course of an infectious disease may be *typical* or *atypical* (the latter case includes forms which are not characteristic of the disease). For example, in persons given inoculations for typhus the disease runs an atypical course; it assumes a mild form with a shortened febrile period.

The febrile period is followed by *convalescence* during which all normal physiologic functions in the organism are restored. However, recovery is not always complete; certain diseases, for example, typhoid fever, sometimes recur. These recurrences—*relapses* take place soon (within 5-20 days) after apparent recovery, or later (within 20-30 days).

Some infectious diseases may run a protracted and sometimes chronic course which lasts for years (chronic dysentery, brucellosis).

It should be remembered that in some cases microbes may remain in the human organism after the acute period of the disease; this is known as *bacteria-* or *microbe-carrying*. In such cases pathogenic microbes may from time to time be excreted into the external environment, owing to which bacteria carriers constitute a serious danger as a source of infection (dysentery, typhoid fever).

The course of an infectious disease is considerably influenced by the patient's age; for example, in old age typhus runs a much severer course and causes serious changes in the cardiovascular system. On the other hand, in 3-10-year-old children typhus usually runs a favourable course. A very important part is also played by the reactivity of the organism.

The clinical course of infectious diseases varies considerably with the individual patients; a particularly important part in the origin of the differences which determine the peculiarities of the individual forms of the disease is played by the functional state of the leading systems of the organism (nervous, cardiovascular and digestive). These peculiarities in large measure emphasize the importance of intoxication of the organism and the degree of development of immunity.

The overwhelming majority of infectious diseases is characterized by febrile reactions of the organism to the invasion of the causative agent; these reactions are well reflected in the temperature curve.

Fever is a defensive and adaptation reaction. Several types of temperature curves are distinguished; these curves may be drawn by marking the morning and evening temperature of the patient on lined paper.

In *continued* fever (*febris continua*) the difference between the morning and evening temperatures does not exceed one degree; such a temperature curve is observed at the height of typhoid fever or typhus.

If the daily temperature variations do not exceed 0.2-0.3 C, they indicate a grave course of the disease and may evidence a serious prognosis.

In *remittent* fever (*febris remittens*) the difference between the morning and evening temperatures often amounts to 2-2.5 C (for example, in brucellosis).

Intermittent fever (*febris intermittens*) is characterized by similarly big differences in temperature, but the high temperatures are *separated* by 2-3-day intervals of normal temperature (for example, in sepsis, malaria). One of the forms of the temperature reaction in infectious diseases is prolonged and exhaustive *hectic* fever (*febris hectica*) which is characterized by sharp differences—3-4 C between the morning and evening temperatures. Such a temperature curve is observed in sepsis.

Undulant fever (*febris undulans*) runs with wavelike rises and drops in the temperature curve for several days and even weeks as may be the case, for example, in brucellosis.

In *recurrent fever* (*febris recurrens*) the period of elevated temperature lasts 4-7 days; it sets in suddenly and ends just as suddenly; after a few days of normal temperature the fever recurs. This type of temperature reaction is observed in relapsing fever.

The various types of curves usually occur in infectious diseases both in their pure form and in combinations for a period of several days. For example, in typhoid fever the undulant temperature curve may end with a period of sharp differences between the morning and evening temperatures (amphibolic).

In infectious diseases the febrile period may end variously. In cases of *crisis* (for example, in relapsing fever) the temperature drops from very high figures to normal in 2-3 hours. In typhoid fever the temperature drops to normal usually very slowly, in stages, over a period of 4-6 days; such a drop in temperature is called *lysis*.

There are also transitional types; for example, in *accelerated lysis* the temperature falls over a period of 1-1.5 days, as is the case in typhus.

Some infectious diseases (for example, tertian malaria) have such a characteristic form of temperature curve that the latter considerably facilitates the diagnosis.

In consideration of the aforesaid it is very important thoroughly to record the patient's temperature on the temperature chart of the case history.

The state of *insusceptibility* of the human organism to a particular infectious disease is called *immunity*. The scientific foundations for studying the processes of immunity were laid by the investigations of the great Russian scientist I. I. Mechnikov (1845-1916), as far back as the 1880's, and were later successfully developed by Mechnikov and other scientists. In 1883, Mechnikov formulated the basic propositions of the phagocytic theory. Although Mechnikov fervently advocated the phagocytic theory he also recognized the important role played by all factors of immunity. The general definition of immunity was also given by Mechnikov in 1903. According to this definition, "insusceptibility to contagious diseases implies the total system of phenomena owing to which the organism may resist the attack of pathogenic microbes".

There are two main types of immunity—natural and artificial. We shall first deal with so-called *natural* immunity.

One of the forms of natural immunity is man's inborn and inherited insusceptibility to a number of diseases; this form of insusceptibility is designated as specific immunity.

Natural immunity also includes insusceptibility possessed by the **newborn** and children in the first 3-4 months of life; these infants

receive *antibodies*, i.e., protective substances, during the intrauterine period through the placenta and after birth with the mother's milk from her organism; the antibodies are capable of safeguarding these infants against certain infectious diseases, for example, diphtheria, during this period. Man acquires a certain degree of *insusceptibility* to a given infection as the result of prophylactic inoculations or by surviving an infectious disease.

The most important form of immunity for medical practice is *active* immunity acquired by man as the result of surviving an infectious disease, for example, typhoid fever; this is also one of the types of *natural* immunity. Many diseases confer a very stable, not infrequently life-long immunity (smallpox, whooping cough, measles, etc.).

Man's insusceptibility to infectious diseases may also be artificial, i.e., the result of *immunization*. For example, if a healthy person is subcutaneously administered a killed culture of typhoid fever bacteria (vaccine), this person will acquire certain insusceptibility to typhoid fever. This is an *active form* of artificial immunity, since the entire organism took active part in its production.

But artificial immunity may also be *passive*. If a person has a wound contaminated with earth which not infrequently contains tetanus bacilli, it is necessary, as soon as possible, to administer to this person subcutaneously a certain dose of serum which neutralizes the tetanus poison (toxin) in the organism. By administering this serum we create in the organism for a relatively short time artificial insusceptibility which is passive since the serum already contains the substances which neutralize the tetanus toxin.

Repeated penetration of small numbers of pathogenic microbes or their toxins into the organism, as may normally be the case, gives rise to a form of immunity owing to which a person subjected to contagion may not contract the particular infectious disease.

In a number of studies conducted since 1883 Mechnikov demonstrated the enormous role played by *phagocytes* (cells which engulf and devour microbes) in the defence of the organism against infectious diseases. He established this role by comparing the processes of intracellular digestion in protozoans (infusoria, sponges) and in higher animals. He found that phagocytes may engulf foreign particles and various microbes and digest them.

In man phagocytes are not only the white blood cells (leucocytes), but also certain immobile cells located in the liver, spleen, bone marrow and connective tissue (elements of the reticuloendothelial system). Mechnikov's basic propositions concerning the role of phagocytosis in the development of immunity are still valid today. Studies conducted by V. K. Vysokovich (1854-1912) and many subsequent authors demonstrated the defensive role of the endothelium of the blood capillaries. Phagocytosis may be clearly observed under the microscope (Fig. 4).

In addition to the phagocytes, an important part in the immunity of the organism is played by special protein substances called *antibodies*. Antibodies are formed in the organism as the result of its active immunization by specific protein substances present, for example, in microbial cells and called *antigens*. In response to administration of microbial antigens or as the result of an infectious process the organism usually produces very specific (acting only on the given microbes) antibodies which may be discovered in the

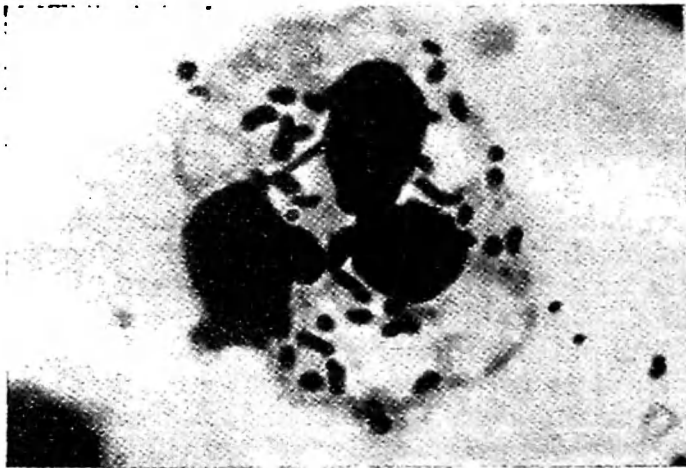


FIG. 1. Picture of phagocytosis of brucellae by neutrophil leucocytes

blood, lymph and tissues of the organism, and which help it to acquire immunity or to overcome the infectious process. In infectious and toxic diseases, for example, diphtheria, the organism produces special detoxicating (neutralizing) substances—*antitoxins*.

Antibodies accumulate in the blood serum of an animal, for example the horse, immunized against a particular microbe or its toxin. This accumulation of antibodies underlies production of therapeutic serums.

In the blood serum antibodies are discovered by means of immune reactions, the most important of which are lysis, agglutination and precipitation.

The *lysis* of bacteria manifests itself in their dissolution under the action of the antibodies contained in the immune serum added to them (action of bacteriolysins).

If we obtain an antigenic extract from a culture of bacteria by boiling this culture with an alkali and, placing this extract in a narrow test-tube, carefully add to the top some specific serum, we shall get at the junction of these liquids an opaque ring of precipitated protein. This reaction is called *precipitation*. It was discovered

by the Russian scientist F. Y. Chistovich (1899) and was soon afterwards used by Uhlenhuth in Germany to determine the specific appurtenance of the proteins of blood plasma.

The reaction of *agglutination* is most widely used in the diagnosis of infectious diseases; the essence of this reaction is the clumping of bacteria and their settling out at the bottom of the test-tube.

Widal's agglutination test is used in the diagnosis of typhoid fever. The serum of the patient's blood dissolved in a physiologic solution in 1:100, 1:200, 1:400 and 1:800 ratios is poured into four test-tubes, one drop of a water suspension of a killed culture of typhoid fever bacteria is added to each test-tube and all of them are placed in a thermostat at a temperature of 37°C. Within 20-24 hours a check-up is made to find the test-tube in which agglutination has taken place, i.e., where the solution has turned colourless and clumped bacteria have settled to the bottom. The greatest dilution of the serum, for example, 1:400, in the test at which agglutination is still noted, is taken as the titre of a positive reaction. The agglutination test is used for laboratory diagnosis of typhoid fever, paratyphoids A and B, brucellosis, tularaemia and, at later stages, also dysentery and many other infectious diseases.

Upon administration of a foreign protein the organism becomes *sensitized* with respect to this antigen and upon repeated administration of the same antigen (for example, therapeutic serum) responds to its stimulatory action differently, i.e., by a more intense local and general reaction due to development of *allergy*.

Allergic states underlie development of urticaria, hay fever and other diseases. The allergy for microbial antigens in man may be established by means of skin tests used in the diagnosis of infectious diseases. Twenty-four hours after intracutaneous administration of 0.1 ml of brucellin (or melitin), which is a filtrate of a broth culture of brucellosis bacteria, to a brucellosis patient a redness, swelling and infiltration (Fig. 5), i.e., an allergic reaction which confirms the diagnosis of brucellosis, may be observed at the site of administration.

A human organism which is highly sensitive to a foreign protein may in some cases respond to repeated administration of the same antigen (for example, therapeutic serum) by a particularly stormy reaction with disturbances in vitally important functions (impaired cardiovascular activity, extreme dyspnoea, convulsions and unconsciousness); sometimes administration of foreign protein may cause death (anaphylaxis, anaphylactic shock). The development of such dangerous conditions is due to the fact that most therapeutic serums are prepared by immunization of horses and, consequently, contain the same foreign protein. Owing to this, serums are administered by the fractional method (p. 75) which prevents development of anaphylactic shock.

Medical practice has completely justified this method.

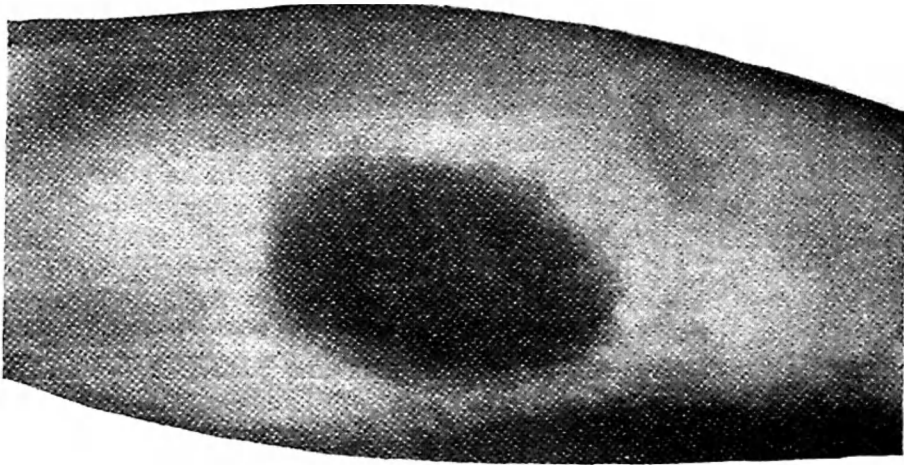


Fig. 5. Burnet's allergic skin test on the forearm

Of late science has acquired a new theory of *autoallergens*; the proteins of pathologically changed tissues may serve as such autoallergens. Sensitization of the organism to these products may apparently play a certain role in the pathogenesis of chronic relapsing dysentery.

CLASSIFICATION OF INFECTIOUS DISEASES

The various infectious diseases are most conveniently classified according to their epidemiologic signs, which makes it possible to characterize *the routes of transmission* of the infections and the associated mechanism of human infection.

The causative agents of infectious diseases may enter the human organism by devious routes:

- (a) through the gastrointestinal tract (intestinal infections);
- (b) through the upper respiratory tract (infections of the respiratory tract);
- (c) through the general blood circulation (infections most commonly transmitted by blood-sucking ectoparasites);
- (d) through the skin and mucous membranes.

The various types of infectious diseases are described in the special part of the textbook in accordance with the foregoing classification. For greater clarity the infectious diseases whose development may be connected with various mechanisms of transmission, and the *zoonotic* infections (transmitted to man from infected animals) are dealt with in chapters according to the basic, most common mechanisms of their transmission.

Intestinal infections. This group of infectious diseases is character-

ized by the fact that on entering man's gastrointestinal tract the infectious principle (causative agent) produces particular clinical and anatomical phenomena.

The infectious intestinal diseases include typhoid fever, paratyphoids A and B, dysentery, amoebiasis, food poisoning, Botkin's disease, cholera, etc.

From the patient's organism the causative agents of intestinal infections are eliminated mainly in the excrements. In cases of infectious intestinal diseases accompanied by circulation of the causative agent in the blood (typhoid fever and paratyphoids) the bacteria may, in addition to the faeces, also be excreted in the urine and saliva.

The pathogenic microorganisms which cause infectious intestinal diseases may gain entrance into drinking water, milk, and food-stuffs, by consumption of which healthy, susceptible persons often contract the disease.

Flies and contamination of human hands with faeces (failure to observe rules of personal hygiene) are not infrequently responsible for the spread of intestinal infections.

The spread of intestinal diseases is controlled mainly by revelation and early hospitalization of patients, disinfection of the foci of the diseases, systematic sanitary supervision over the water supply and sewerage, observance of the rules of food and personal hygiene, and extermination of flies. Preventive inoculation is only of auxiliary importance.

Respiratory infections. The infections of this group include the diseases whose causative agents parasitize on the mucous membranes of the upper respiratory tract (nose, pharynx and larynx); the causative agents of these diseases are eliminated from the patient's organism into the external environment by forcible exhalations (coughing or sneezing). Minute particles of mucus containing pathogenic microorganisms (bacteria, filtrable viruses) are discharged from the oral cavity and the nose during coughing, sneezing and even talking.

A healthy person becomes infected on close contact with a patient when infected particles of mucus may easily enter the upper respiratory tract. Owing to this mechanism of transmission of respiratory infections the latter are often called *droplet* infections. In some cases minute droplets of mucus are discharged from the nasopharynx into the air and may be carried from one room into another with the result that the elementary particles of filtrable virus (causative agent) gain entrance into the upper respiratory tract of healthy, susceptible people and infect them.

The mechanism of transmission of respiratory infections makes possible their extensive epidemic spread, especially among children.

Some infections of this group—influenza, measles, whooping cough—are characterized by the fact that the pathologic processes

develop at the point of entrance of the causative agent; smallpox, chickenpox (varicella) and epidemic meningitis are diseases whose causative agents may penetrate from the portal of entry into the blood and may affect the skin, mucous membranes and the central nervous system.

The same group of respiratory infections includes diphtheria, scarlet fever and epidemic parotitis (mumps). But these diseases, in addition to the air-borne or droplet method of transmission, are also transmitted through various objects (for example, toys) infected with particles of mucus from the upper respiratory tract of a patient or carrier.

The control of respiratory infections includes isolation of patients and measures of personal precautions (for example, wearing gauze masks which cover the mouth and nose of the healthy person attending to an influenza patient). A decisive role in preventing smallpox is played by highly effective inoculations (vaccination and revaccination).

General circulation infections. These diseases are classified according to their common factor, i.e., penetration of the causative agent into the bloodstream of a healthy person through bites by infected blood-sucking insects (lice, fleas, mosquitos, sandflies, ticks) with subsequent parasitism of the causative agent on the erythrocytes (malaria), the endothelium of the capillaries (typhus and a number of other rickettsioses), or the central nervous system (tick-borne encephalitis, etc.).

It should be emphasized that the causative agents of this group of infectious diseases have adapted themselves, in virtue of evolution, to parasitizing not only on the human organism, but also on the organism of the carriers of the infections.

As an example of this type of infectious diseases mention may be made of typhus which is caused by *the Rickettsia prowazeki*; this causative agent multiplies in the cells of the intestinal epithelium of body lice which serve as carriers of this infection from man to man. Certain biological characteristics of the carrier of an infection, for example, the mass flight of the *Anopheles* mosquitos which transmit malaria to man, are connected with factors in the external environment (certain time of the year, temperature of the air, humidity, presence of reservoirs, etc.) and determine the seasonal character of the particular infectious disease.

Tick-borne encephalitis which belongs to the same group of diseases is also a seasonal disease since the *Ixodes* ticks which are carriers of the infection attain maturity in May-June and, by attacking man, may infect him with encephalitis at that time of the

Many diseases of this group (for example, tick-borne relapsing fever, seasonal encephalitides, and many others) have *natural foci*; the carriers of these diseases may exist only under certain geograph-

ical, climatic and soil conditions or where there is corresponding vegetation. This determines the concept of *biotope*, i.e., the concrete conditions of the carrier's habitat. The theory of natural foci of infectious diseases was brilliantly worked out by Academician E. N. Pavlovsky.

The preventive measures against these infections consist in neutralization of the sources of infection; applied to patients, as sources of infection, it means their hospitalization and treatment. It is also necessary to exterminate the blood-sucking carriers and to protect healthy people from bites of parasites.

Infections of the skin and mucous membranes. These infections are transmitted by their causative agents passing from patients or diseased animals, on which they parasitize, to the skin or mucous membranes of healthy susceptible persons.

This group of infections includes anthrax, glanders, foot-and-mouth disease, tetanus, erysipelas, trachoma and a number of other diseases. In these diseases the infectious principle is transmitted from the source of infection both directly and through infected objects; for example, a person may contract anthrax through a fur collar infected with anthrax bacteria, a typical anthrax carbuncle forming on the person's face or neck.

Control of infections of the skin and mucous membranes consists mainly in isolation and treatment of patients and disruption of the routes of transmission; an example of the latter is manufacture of footwear only from leather subjected to special control with respect to its contamination with anthrax spores. Inoculations used to prevent tetanus and anthrax play an auxiliary role. Diseases whose causative agents gain entrance into the organism of a healthy person through damaged skin or mucous membranes (traumatic infections—erysipelas, tetanus) constitute a special variety of this group of infections.

In addition to the aforementioned categories of infectious diseases there are also others with more complicated, multiform and as yet insufficiently understood mechanisms of transmission. These diseases include acute epidemic poliomyelitis, although it is already well known that it is transmitted mainly by the causative agent gaining entrance into the gastrointestinal tract, for example, through consumption of virus-infected milk.

By reason of a number of epidemiologic peculiarities a special group of so-called "zoonotic infections" is often distinguished: these are infectious diseases transmitted to man from diseased animals (brucellosis, tularemia, anthrax, etc.). The author deemed it necessary to describe the zoonotic infections in a special chapter in order to facilitate the study of the main methods of diagnosis, the clinical picture, treatment and prevention of these diseases. It should be remembered that these diseases may be transmitted by any of the afore-described mechanisms.

PRINCIPAL METHODS OF DIAGNOSING INFECTIOUS DISEASES

It is often very difficult to diagnose infectious diseases, especially at early stages of their development. Only a thorough examination of all the clinical, epidemiological and laboratory data, as well as of the results of special tests (for example, X-rays of the lungs and skin allergy tests in the bronchopulmonary form of tularaemia) makes it possible to establish a correct diagnosis of an infectious disease.

Attempts should be made during the very first examination of a patient to elucidate all the epidemiological data which may facilitate the diagnosis of an infectious disease. During this examination the physician must take into consideration the infectious diseases the patient has survived, the preventive inoculations, the patient's contacts in the last 25 days with infectious patients or bacteria carriers, the existence of epizootics in the given area, the sanitary, hygienic and natural conditions under which the patient has of late been living, the observance of personal hygiene by the patient, discovery of ectoparasites on the patient, his underwear or clothing, traces of bites (of animals or blood-sucking parasites) and primary effects at the site of penetration of the infection.

In case of suspicion of epidemic hepatitis (Botkin's disease) whose incubation period may last 6-8 weeks, and in the event of parenteral infection (through a syringe)—up to six months, it is necessary to check up carefully on the patient's contacts with other patients, the injections being given to the patient and the blood taken from him during the indicated period. If the patient's examination leads to suspicion of tetanus, it is necessary to ascertain if the patient has had any injuries or wounds in the skin during the preceding 2-3 months, especially injuries or wounds involving contamination with earth. The maximum duration of the incubation period of the particular infectious disease must always be borne in mind. It is necessary to record all the aforementioned information concerning the epidemiological anamnesis in the case history with which the patient is admitted to the hospital. Similar information must also be carefully collected in the reception division of the infectious hospital from the patient himself, his relatives and escorts.

Special attention must be devoted to the patient's anamnesis—his complaints and earliest symptoms of the disease observed by the patient himself and the people around him (chills, vomiting during the first hours of the disease, loss of consciousness, etc.).

This must be followed by collection of information which characterizes the patient's condition at the given moment. All the information thus received must be recorded in the case history.

The patient's neuropsychic condition and state of consciousness (excitement, stupor, coma, extreme inhibition, unconsciousness, delirium, aggressiveness, etc.), as well as the complaints of certain

pains (for example, upon movement of the eyeballs in influenza patients or in the gastrocnemius muscles during relapsing fever) are very important for diagnosing many infectious diseases.

Examination of normal and pathologic reflexes, and elucidation of meningeal symptoms supplement the picture of pathology of the infectious patient's nervous system.

Examination of the skin and visible mucous membranes may yield important symptoms for the diagnosis of infectious diseases. For example, typhus is characterized during the first 3-4 days by hyperaemia and puffiness of the face, and injection of the vessels of the sclerae and conjunctivae; a roseolous or roseolous-patechial polymorphous eruption localized mainly on the lateral surface of the chest and on the flexor surface of the arms appears on the fourth, fifth or sixth day of typhus.

A roseola is a small (2-3 mm in diameter) rose-coloured spot on the skin and disappears when the skin is stretched; it is formed as a result of inflammatory changes and dilatation of small vessels. A roseola may have a regular form, round (in typhoid fever) or elongated, with festooned, serrated edges (in typhus).

Petechiae are haemorrhages into the skin; they appear as small red points which do not disappear upon stretching of the skin or pressure exerted on it (in typhus, sepsis).

A papular eruption which appears in measles patients consists of a number of small round rose-coloured lesions elevated above the surface of the skin. Some infectious diseases are accompanied by formation on the skin of vesicles filled with a colourless (chicken-pox) or purulent (smallpox) substance; the latter are called pustules.

Characteristic eruptions appear on the oral mucosa in measles during its prodromal period (Belsky-Filatov-Koplik's sign) and in the foot-and-mouth disease (aphtha epizootica).

The symptoms of affection of the skin and subcutaneous tissue at the portal of entry of the infection are of paramount importance; these symptoms constitute *the primary affect* which may be: (1) a large brown papule caused by the bite of a tick in cases of infection with tick-borne rickettsiosis; (2) formation of ulcers on the skin in cutaneous leishmaniasis and ulcerative bubonic tularaemia; (3) characteristic anthrax carbuncle, etc.

Many infectious diseases are characterized by an enlargement of regional (at the site of penetration of the infection) lymph nodes (tularaemia, bubonic plague).

In a number of cases infectious diseases are accompanied by affection of the joints. For example, the formed clinical picture of brucellosis, especially during the local affection stage, is characterized by limited mobility, pains in large joints and their enlargement. Fibrositides, cellulitides, and bursitides are symptoms often observed in subacute and chronic brucellosis.

Clinical and roentgenological examinations of the respiratory

organs and analyses of the sputum make it possible to discover facts which are very important for the diagnosis of pulmonary forms of anthrax, tularaemia and the plague.

Examination of the infectious patient's cardiovascular system permits of discovering a number of essential symptoms. For example, in typhoid fever patients the pulse rate lags behind the temperature level (relative bradycardia) and a dicrotic pulse is often observed during the febrile period.

During examination of the fauces special attention is devoted to the condition of the mucous membrane of the mouth, the tonsils, the hard and soft palates. The presence of fine branlike scaling on the mucous membrane of the cheeks (Belsky-Filatov-Koplik's sign, see "Measles") is an important diagnostic sign of measles in the prodromal stage. Separate greyish-white "islets", i.e., dense films of fibrin on the tonsils, should make the physician suspect primarily faucial diphtheria. An enlargement of one of the tonsils with a superficial necrotic film on it and regional (submaxillary) lymphadenitis warrant suspicion of the anginous-bubonic form of tularaemia.

No less important for diagnosis is the examination of the tongue. An oedematous, enlarged tongue with imprints of the teeth along its edges and a greyish film on its dorsal aspect so that its edges and tip are clear and red, is a very characteristic symptom of typhoid fever; the appearance of the tongue is also typical in the plague ("chalk" tongue) and on the third day of scarlet fever (Fig. 6). In examining the patient's abdomen it is necessary to observe its size, configuration (inflated or sunken) and tenderness on palpation of any of its parts. An inflated abdomen (meteorism) due to accumulation of gases in the intestines is very characteristic of typhoid fever. Pain and spasm of the sigmoid colon are observed in dysentery; a rumbling in the right iliac region on palpation is characteristic of typhoid fever.

Many infectious diseases are characterized by an enlargement of the liver and, especially, of the spleen, as organs containing many reticuloendothelial elements, since the reticuloendothelial system directly participates in the development of a number of infectious diseases. The spleen is particularly enlarged in malaria, relapsing fever and leishmaniasis.

A careful and complete clinical examination of the patient and utilization of various methods of functional diagnosis (including rectoscopy for examining the lower portion of the large intestine of dysentery patients, or an X-ray picture of the lungs in the pulmonary form of tularaemia), taking into consideration the dynamics of the appearance, increase and abatement of the clinical symptoms yield data which are very important for diagnosing infectious diseases.

Speaking of the fundamentals of diagnosis of infectious diseases we must not overlook the factors which have of late exerted an es-

stantial influence on the clinical symptomatology of these diseases and must necessarily be taken into account in establishing a diagnosis.

Today some infectious diseases which still occur in the USSR essentially differ in their clinical course from that observed in the past (about 20-50 years ago). These differences are due primarily to the increase in the general reactivity and resistance of the human organism brought about by improved living standards of broad sections of the population. *In recent years the clinical picture of a number of diseases has changed* because of extensive inoculations which have not only sharply reduced the total incidence of diseases, but in cases where diseases have developed just the same have contributed to their favourable course (atypical, erased forms). *These peculiarities are as much as possible dealt with in this textbook.*

In discussing the modern course of various infectious diseases it should be especially emphasized that the clinical picture of dysentery changed already in 1937-1942 owing to the altered aetiology of the disease, disappearance of the toxigenic strains of the Gligoryev-Shiga bacilli and as the result of extensive administration of sulpha drugs (and subsequently antibiotics).

The sporadic cases of typhus observed since 1948 over a period of several years ran a milder course than those which were typical of the classical forms of this disease. This fact must be considered due primarily to the increased general resistance of the Soviet people to infections as the result of the steady rise in their living standards. The diminished virulence of the causative agent of typhus (*Rickettsiae prowazeki*) because of its fewer passages through the human organism, as well as the diminished infective dose are due to infrequent and unintensive cases of pediculosis and the increased life span of the infected lice; these factors have in their turn determined the milder course of typhus in the cases observed since 1948. It must also be remembered that owing to the varying immunity of a collective the course of the self-same infectious disease (for example, diphtheria) may essentially vary.

Of the various methods of laboratory diagnosis an important role is played by clinical tests of the blood and urine. An increase in leucocytes in the blood accompanied by an increase in the percentage of neutrophils and a shift of the leucocytic formula to the left is characteristic of typhus and a number of other infections. At the same time a decrease in the total number of leucocytes (leucopenia) with relative lymphocytosis and absence of eosinophils in the blood characterizes typhoid fever at its height.

Typical changes in the blood picture (total amount of leucocytes and the leucocytic formula) may be established in many infectious diseases. Changes in erythrocytes are observed somewhat less frequently. Considerable hypochromic anaemia is noted in various infections, for example, in visceral leishmaniasis.

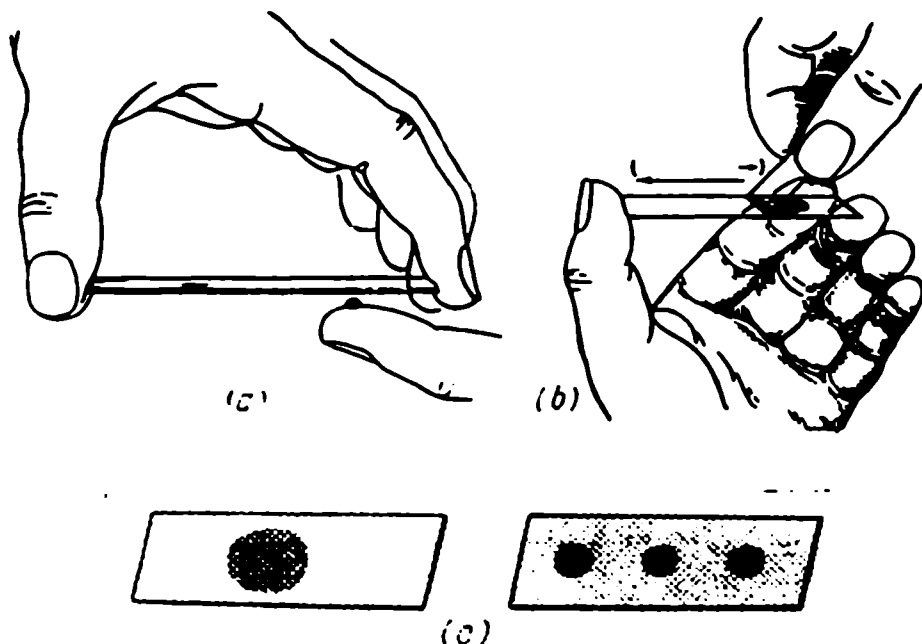


Fig. 7. Taking blood on a slide (a), preparation of a smear (b) and of a thick drop (c)

Examination of the urine of infectious patients often reveals but a slight febrile albuminuria. However, in such diseases as icteric leptospirosis (Weil-Vasilyev's disease) or haemorrhagic nephrosonephritis, marked albuminuria, haematuria and cylindruria are observed.

An important role in the establishment of a diagnosis is played by an analysis of the temperature curve which in many infectious diseases (measles, smallpox, relapsing fever, tertian and quartan malaria, etc.) shows certain peculiarities.

To confirm the diagnosis of infectious diseases the modern clinic makes extensive use of a number of specific laboratory tests.

Although sparingly used, the bacterioscopic method constitutes a very important part of diagnosis; this method is aimed at finding the causative agents of infectious diseases in the blood of patients with the aid of microscopy of stained blood preparations (smears, or thick drop of blood, Fig. 7). This microscopic method of laboratory diagnosis is used particularly in diagnosing relapsing fever (to discover spirochaetes in the blood) and malaria (to find plasmodia in the erythrocytes) and is very important for confirming the diagnosis in cases where the causative agents of these diseases have been discovered.

The possibilities of bacterioscopic diagnosis are considerably ex-

Haematological sign	Observed in
Moderate hypochromic anaemia.	Typhoid fever, paratyphoids A and B, epidemic hepatitis (Botkin's disease), fresh cases of malaria, infectious mononucleosis, incipient stage of visceral leishmaniasis.
Severe hypochromic anaemia.	Protracted forms of malaria, visceral leishmaniasis at later stages of its development.
Hyperchromic anaemia.	Acute tuberculous sepsis (in some cases).
Normocytosis with neutrophilia and lymphopenia.	Water fever; about 15-20 per cent of typhus cases.
Leucopenia with neutropenia and relative lymphocytosis.	Botkin's disease, influenza, brucellosis, malaria, typhoid fever, varicella, measles.
Leucopenia with monocytopenia	Recurrent fever (in the stage of apyrexia).
Leucopenia with neutropenia, relative lymphocytosis and monocytosis.	Malaria, visceral leishmaniasis; during the first two days of the disease leucopenia is observed in haemorrhagic fever with a renal syndrome.
Leucocytosis with lymphocytosis or lymphomonocytosis.	Whooping cough, infectious mononucleosis (mononucleosis patients with leucocytosis exhibit mononuclear, broad-plasma leucocytes with basophilic granularity in the protoplasm).
Leucocytosis with moderate monocytosis.	Recurrent fever.
Leucocytosis with neutrophilia and nuclear shift of leucocytes to the left.	Typhus (80-85 per cent of the cases), erysipelas, icterohaemorrhagic leptospirosis, epidemic and pneumococcal meningitis, haemorrhagic fever with renal syndrome (beginning with the 3rd day of the disease), scarlet fever, recurrent fever (during attacks).
Eosinopenia and aneosinophilia.	Influenza, measles, varicella, infectious mononucleosis, typhus, paratyphoids A and B, typhoid fever (as a rule, aneosinophilia), recurrent fever.
Eosinophilia.	Scarlet fever, trichinosis.
Fast erythrocyte sedimentation.	In most cases of acute infectious diseases with an active pathologic process.
Slow erythrocyte sedimentation.	Epidemic hepatitis (Botkin's disease).
Moderate reticulocytosis.	Some cases of visceral leishmaniasis.
Thrombocytopenia.	Typhoid fever, paratyphoids A and B, typhus, recurrent fever (during attacks), haemorrhagic fever with renal syndrome, smallpox.
Türk's irritation cells.	Some cases of typhus, haemorrhagic fever with renal syndrome.
Plasma cells.	Recurrent fever (mainly during attacks), smallpox.

tended owing to the use of fluorescent antibodies (after Coons) with subsequent use of a fluorescence microscope.

The *bacteriological* method of diagnosis is rather widely used; this method is based on isolation of the causative agents from the patient's blood, bile, urine or faeces, which are inoculated in special nutrient media; the bacteriological method is used particularly for confirmation of the diagnosis of many infectious intestinal diseases (typhoid fever, food toxoinfections, dysentery; see Supplement 2). It should be noted that the use of this method is limited by the lack of suitable nutrient media and the difficulty of isolating the causative agent from the patient's organism in many infectious diseases, especially those caused by filtrable viruses.

The aetiology of an infectious disease may also be judged by indirect—immunological—indices. Of the immunological methods of examination now in existence *serological* tests (from the word *serum*) are the most widely used; these tests are based on discovery of antibodies (most commonly agglutinins) for the killed culture of the causative agent of the particular infectious disease in the serum of the patient's blood. Agglutination tests, whose technique is very simple, are used particularly frequently.

Agglutination tests are used in typhoid fever (Widal's test), brucellosis (Wright's test) and many other infectious diseases. A characteristic feature of agglutination tests is that they become positive not during early periods of a disease, but only at its height, the titre increasing with the progress of the disease.

Diagnoses of various infectious diseases may also be confirmed by *allergic* skin tests. For a skin test 0.1 ml of a diagnostic preparation (for example, in brucellosis—brucellin which is a filtrate of a three-week broth culture of brucellae) is injected with a thin needle into the skin. In the presence of the disease a hyperaemic area surrounded by an infiltrative ridge forms at the site of brucellin administration (positive allergic reaction) 24 hours after the Burnet test (see Fig. 5). A similar allergic method of diagnosis may be used in other diseases, for example, in tularaemia; for this purpose 0.1 ml of tularin (a suspension of killed tularaemia bacteria) is administered intracutaneously.

In establishing a diagnosis of an infectious disease it is necessary to take into account the possible area of geographic distribution of the disease (leishmaniasis, pappataci fever and other infectious diseases which have their natural foci). The geographic distribution of pappataci fever and leishmaniasis completely excludes the possibility of contracting these diseases in the central and northern areas of the USSR. It is therefore entirely unnecessary to establish a differential diagnosis of this disease in the aforementioned areas except in cases of new arrivals from the southern areas of the country where these diseases occur). At the same time such a disease as tick-borne encephalitis may occur not only in the taiga



Fig. 6. Tongue of a child, fever patient: left — on the 1st day, and right — on the 3rd day of the disease.

regions of Siberia, but also in the Udmurt ASSR and in certain other parts of the country. Haemorrhagic nephrosonephritis occurs not only in the Far East, but also in the Urals, in the Kalinin, Yaroslavl, Tula and other regions. That is why it is so important to know the nosogeography of infectious diseases.

ORGANIZATION OF AND REGIMEN IN CONTAGIOUS HOSPITALS AND DEPARTMENTS

Purpose of Contagious Hospitals (Departments)

To isolate infectious patients for the entire period of their actual contagiousness and to treat them, there are special *contagious hospitals* or *contagious departments* of hospitals. All infectious patients must be hospitalized without fail, except those who may be treated at home (cases of measles, influenza).

The organization of and regimen in contagious hospitals (departments) must ensure complete isolation of patients, who are sources of infection, and must provide proper therapy; at the same time it is necessary to take measures to prevent intrahospital infection.

It is absolutely obligatory to observe the following most important rules in hospitalizing every infectious patient.

1. Correct primary diagnosis in the admission department of the hospital, necessarily establishing all contacts the patient may have had with other infectious patients; strict individual hospitalization in wards (compartments) of all persons affected with mixed infections and those who had contact with other very infectious patients (for example, measles patients).

2. Appropriate sanitation of every patient upon admission to the hospital or department.

3. Placement of patients in wards according to the character of the disease, and thorough current disinfection.

4. Prevention of other infections from being brought into the department or ward.

5. Administration of medical treatment.

6. Ascertainment of the absence of contagion in convalescents being discharged from the department (bacteriological analysis to reveal infection-carrying).

General Organization and Lay-out of Contagious Hospitals (Departments)

In addition to an admission department and several departments intended for distribution of patients according to their diseases, each contagious hospital must have showers, disinfection chambers and a laundry. If the contagious department occupies only part of

the hospital building, it must have its own showers, disinfection chamber and laundry. If the hospital does not have a central water supply system and sewerage it must have a clean well and provisions for collecting and neutralizing the excrements.

The auxiliary building, including the food department (store-rooms for foodstuffs, kitchen and pantry) must be located on the hospital grounds in separate units at requisite distances from the therapeutic buildings.

It is advisable to house the contagious departments in separate buildings—*pavilion system*; patients affected with the same disease, for example, dysentery, are placed in one of these departments or in several neighbouring wards. In cases where a contagious hospital occupies a one-, two- or three-storey building the departments intended for hospitalizing similar infectious patients must be located on separate floors. Patients with air-borne infections, for example, measles, scarlet fever, etc., should be placed in the upper storeys.

In the Soviet Union typical district or local contagious hospitals consist of separate buildings accommodating 10-20 patients each. A 20-bed district hospital consists of two sections intended for hospitalizing patients with various nosological forms of diseases.

According to standard hospital designs, each section consists of one-bed, two-bed and three-bed wards, two separate compartments, showers for patients, showers for the personnel, a pantry, a separate room for washing the bedpans, a linen room for clean linen and one for soiled linen, a room for the physician on duty, and rooms for the intermediate and junior medical personnel.

In a contagious hospital (department) patients with different diseases must not be allowed to associate with each other; nor must the members of the staff attending to different departments be allowed to associate with each other. The food is delivered to the pavilion from the central hospital kitchen and is then heated in the pantry of the department.

Each ward must admit patients only with the same disease. Whenever it is impossible to establish the correct diagnosis in the reception room, the patients suspected of typhoid fever, typhus, malaria, brucellosis, tularaemia, etc., are placed in so-called *temporary distribution wards*; after ascertainment of the diagnosis (within 2-3 days) these patients must be transferred to wards in accordance with their diseases.

Patients with *mixed* infections (for example, typhus and aggravation of chronic dysentery) must be placed in individual wards; the same must be done with patients who had contact with persons suffering from other infectious diseases.

Infectious patients are admitted to hospitals and placed in wards or separate compartments on the basis of a system which prevents their association with patients suffering from other infectious diseases and are kept there until discharged.

In accordance with the principles of this system, in contagious hospitals patients undergo primary sanitary treatment (disinfection and disinsection of their personal effects and detoxication of their excretions) and rational medical treatment, and after final disinfection and a check-up on bacteria-carrying are discharged from the hospital.

Each patient referred to a contagious hospital is first admitted to the reception division.

Work of the Admission Department

In cases where a hospital consists of separate pavilions the admission department occupies a whole building; if the hospital is housed in one building, the reception division must occupy absolutely isolated premises (Fig. 8).

Infectious patients delivered by ambulance are admitted to separate compartments intended only for definite types of diseases (for example, for admission of typhoid fever patients, scarlet fever patients, diphtheria patients, etc.). The compartment in which the new patient is examined must have its own entrance and exit. It is desirable that the entrance to and the exit from the compartment should not be in the street, but in the hospital yard. In addition, each compartment must have double glass doors into the corridor of the admission department; all the doors of the separate compartments must be locked and the keys kept by the personnel on duty. The arrangement of the compartment enables the physician on duty to examine the patient directly in the compartment whence the patient is placed in the requisite division of the hospital without coming in contact with other patients and, consequently, without spreading the infection or being subjected to the danger of additional contagion. Each compartment must have robes for the personnel,

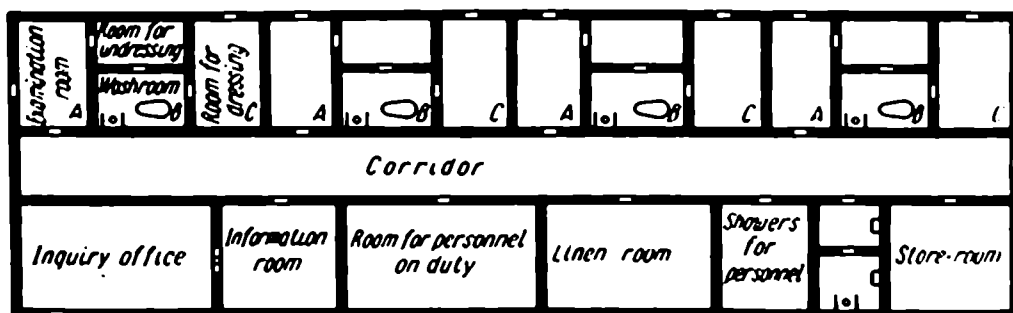


Fig. 8. Admission department of a contagious hospital (with several sections)

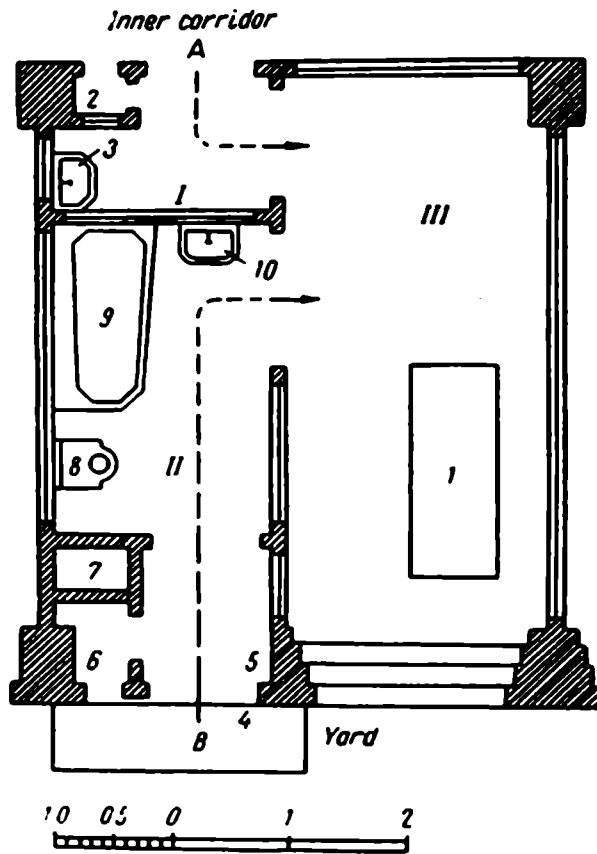


Fig. 9. Complete Meltzer compartment

I—entrance for personnel; B—entrance for patients; I—passage-way for personnel; II—passage-way for patients; III—ward
1—bed; 2—window for passage of food; 3—washstand for personnel; 4—porch; 5—antechamber; 6—place for dirty linens and dishes; 7—ventilation shaft; 8—toilet bowl; 9—bath-tub; 10—washstand for patient

a couch, a desk, chairs, a closet with an assortment of medicaments for first aid, syringes with needles, a sterilizer and apparatus for tests (sterile tampons in test-tubes for taking smears of mucus from the fauces for diphtheria, a conserving mixture in test-tubes for taking excrements to be tested for dysentery bacteria, etc.)

The admission department must have special *therapeutic compartments* or one- and two-bed wards well isolated from the other premises and intended for isolating patients with mixed infections.

Children suffering from infectious diseases are examined upon admission to the hospital in special Meltzer-system "through" compartments (Fig. 9). Each compartment consists of an antechamber to which the patient is admitted, the compartment proper with a bathroom and toilet, and an inner chamber containing robes and a

washstand for the personnel. The attending personnel enter and leave the compartment, food is brought to the patient, etc., through the inner chamber which communicates with the corridor through tightly-closing, partly glazed doors. The Meltzer compartment must have hot water bottles, enemas, bedpans, rubber rings, ice-bags, catheters, linen, medical instruments, etc.

In addition to admitting new patients, Meltzer compartments may also serve for individual hospitalization of patients with airborne or other very contagious diseases. In such cases the patients stay in the compartment until they are discharged from the hospital. The discharged patients leave the compartment through the exit (to the hospital yard), and a final disinfection is made in the compartment.

Proper organization of the admission department, strict isolation of patients in accordance with the diagnosis, appropriate sanitary treatment, and the availability of compartments for isolating patients with mixed infections ensure effective control of intrahospital infections.

An extremely important part in preventing intrahospital infections is played by elucidation of *the epidemiological anamnesis* since it facilitates a diagnosis of the given disease and helps to find out whether or not the patient had contacts with other infectious patients, owing to which a *mixed* infection is possible.

In collecting the epidemiological anamnesis, especially in cases of sick children, it is first necessary to determine the infectious diseases, including measles, scarlet fever, epidemic parotitis, whooping cough and varicella, which the given patient may have survived (since these infections confer permanent immunity and rarely recur).

It is no less important to find out about *the contacts* the patient may have had with other infectious patients over a period of 3-4 weeks preceding the present disease. This is particularly important with respect to measles, varicella, whooping cough, scarlet fever, diphtheria and epidemic parotitis. It is necessary to find out about all types of contacts with acutely infectious patients in the family, house, children's institution, etc. Such a contact over a period of 22-23 days (longest incubation period of any infectious disease) preceding admission to the hospital warrants the assumption that the given patient is in the incubation period of the infectious disease with which he had contact. Such cases require *individual* isolation in special Meltzer compartments or small wards intended for one or two patients.

A careful examination makes it possible to reveal patients suffering from *mixed* infections, for example, measles and diphtheria, varicella and whooping cough. Patients with signs of mixed infections are placed in separate compartments (preferably Meltzer compartments) or in small isolation wards.

Strict observance of the aforesaid rules for isolating patients

and the placement of these patients in divisions corresponding to their diseases are absolutely obligatory for all contagious hospitals. Admission departments must employ well-trained medical personnel.

Every patient admitted to the admission department of a contagious hospital is carefully examined by a physician or assistant physician who, taking into consideration the epidemiological anamnesis and the patient's covering documents, diagnoses the disease and after sanitary treatment refers the patient to the corresponding ward or isolation compartment. In the admission department a case history is started for every admitted patient. The case history includes the results of the examination, all the items contained in the covering documents and all information received from the patient's escorts. Simultaneously the patient's personal effects retained in the hospital are recorded on a special blank, and the kitchen is notified concerning the patient's diet.

During the patient's examination in the admission department the physician (or assistant physician) on duty prescribes the necessary sanitary treatment for the patient (bath, shower, or only moist sponging, obligatory removal of the hair or only treatment of the hairy parts of the head with insecticides) and indicates the method of delivering the patient to the ward (on a stretcher, wheel-chair or on foot). Some infectious patients are extremely excited, in which case they are put under special supervision of the medical personnel. In the case history the physician (or assistant physician) on duty records the first prescriptions and indicates the tests which must necessarily be performed during the very first hours after hospitalization. Smears of mucus are taken with a sterile tampon without fail from the fauces and nose of all children for a check-up on diphtheritic bacteria-carrying.

The newly admitted infectious patients are given the following sanitary treatment: the hair on the head, symphysis pubis and in the arm pits is removed or treated with a 5 per cent DDT soap, or with a 10 per cent albichtol (white ichthyol) paste; the removed hair is burned.

If the patient's condition permits, the patient is given a shower or bath. Debilitated patients are given a sponging with warm water to which either toilet water or 0.5 per cent vinegar is added. The nails on the fingers and toes are trimmed. After the sanitary treatment of each patient the sponges and wash-clothes are boiled, and the bathtubs and shower rooms are washed with hot water.

After the shower or bath the patient enters the dressing room adjacent to the admission department and is given clean underwear.

The patient's own underwear is put in an individual tightly fastened and numbered bag which is sent to the laundry where it is soaked in a 0.5 per cent chloramine solution after which it is boiled and washed with soap. Instead of soaking in chloramine the under-

wear is sometimes boiled in lye. If the patient's underwear contains lice, it is treated with a 5 per cent DDT soap or a 3 per cent hexachlorocyclohexane soap. The newly admitted patient's outer garments are placed in a tightly fastened bag and are sent to the disinfection chamber.

From the admission department the patients are referred to corresponding divisions of the hospital where they are placed in wards in accordance with their diseases. Patients found to have no acute infectious disease (for example, measles, varicella, diphtheria) are placed in preliminary distribution wards. After establishment of the diagnosis patients are transferred from distribution wards to common wards in accordance with their diseases. Only patients with mixed infections or those who are in the incubation period of a concurrent infectious disease are left in special compartments.

The admission department usually houses the section of medical statistics of the hospital and the archive of case histories; it also has a room for issuing certificates concerning the condition of the patients. The admission department must also have showers for the personnel on duty.

Work of a Contagious Department

Each contagious department sets apart 2-3 (or more) one- or two-bed wards for the purpose of isolating the gravest cases and for nosocomial (intrahospital) infections.

Certain rules of hygiene must be observed in setting up wards in contagious departments. The size of the wards must allow 6-7 sq m of space per patient with a distance of at least 1 m between beds. Each patient must have 18-22 cu m of space. The temperature in the wards must be close to 18°C with a relative humidity of not more than 50-55 per cent.

The wards must have adequate natural lighting and effective ventilation. The simplest form of ventilation is provided by transoms in the upper part of the windows. In winter the transoms are opened for 10-15 minutes every two hours, the patients being warmly covered with blankets. In summer it is desirable to keep the transoms open 24 hours a day.

The requisite sanitary and hygienic conditions in the department are maintained by regular cleaning of the wards and all other premises, disinfection and disinsection, regular bathing of the patients, changing of the underwear and linens, and strict observance of the rules of personal hygiene by both the attending personnel and the patients.

Every patient, his condition permitting, must take a weekly bath or shower; in severe cases the bath or shower is replaced by sponging.

An important part in the work of a contagious hospital is played by the disinfection service; the functions of this service are performed by disinfection specialists for the entire hospital and by the personnel of each department for the departments.

The functions of the disinfection service of a hospital consist in:

(1) sanitary treatment of all patients admitted to any department, including disinsection and disinfection of their personal effects;

(2) disinfection in departments, including current and final disinfection at the patient's bedside, bathrooms, toilets, and auxiliary premises, as well as extermination of ectoparasites and rodents;

(3) detoxication of sewage, cesspools and garbage cans.

For proper disinfection the hospital must have enough disinfection chambers, apparatus for moist and gaseous disinfection and for spraying insecticides, and a constant stock of disinfectants including chloride of lime, chloramine and insecticides (DDT powders and soap and hexachloran [hexachlorocyclohexane]). Immediately after the delivery of a patient to the admission department the ambulance must be disinfected, which is particularly important in cases of very contagious diseases.

The patient's underwear soiled with faeces or urine must be changed immediately, soaked in a 0.5 per cent chloramine solution, then boiled and laundered. Everything used by the patient (including bedpans, hot water bottles, rubber rings, towels, handkerchiefs, etc.) must be strictly individual. All these things must be disinfected according to the foregoing rules.

In children's contagious departments the patients may be allowed to play only with rubber or celluloid toys which can be easily disinfected.

Each toilet must have containers with a 10 per cent chloride of lime solution for disinfecting the bedpans, and wooden shelves for keeping the individual bedpans. The toilet bowls and toilet seats must be washed four times a day with a 0.5 per cent chloride of lime solution. The floors in the wards must be swept twice a day with brushes wrapped in moist cloths; the corridors and all auxiliary premises must be cleaned in a similar manner. The corridors must be aired periodically.

The windows of the wards and all auxiliary premises must be screened with a wire mesh for the entire warm season of the year to prevent flies from penetrating into the premises. Good results in the control of flies are produced by dusting the windows with 2 per cent hexachlorocyclohexane powders or by spraying with a 2 per cent DDT solution (in the latter case 100 ml of the solution is used per 1 sq m of surface). As a rule, it is enough to carry out such insecticidal measures twice during the entire summer season to have no flies in the hospital.

The food for the patients must be prepared in the central kitchen which caters to the entire hospital. The food brought to the department from the central kitchen must be heated, apportioned for distribution to the patients in *the food department* which must be completely isolated from the wards and other premises. The food department must consist of a pantry and a room for washing the dishes. The food must be heated on a stove (in large hospitals the food must be delivered from the kitchen in thermos bottles) for which aluminium, enamelled or stainless steel pots and pans must be used. The pantry must have a separate entrance. The food must be handed to the hospital attendants through a little window which opens from the pantry into the corridor. The soiled dishes must be placed for one hour in a 0.5 per cent chloramine solution after which they must be boiled. The food remains must be placed in an iron box, topped with chloride of lime, covered with a lid and after two hours must be thrown into the sewerage or a cesspool.

After boiling the dishes must be dried on wooden grates (without the use of towels).

Special rooms must be set apart for storing the utensils, clean and soiled linens (separately).

The contagious department must also have rooms for the physician (or assistant physician) and other medical personnel on duty, a room for the head of the department, cloak-room for the personnel with individual lockers for their clothes and separate lockers for the robes.

The physician (or assistant physician) on duty must have at his disposal a locker with first-aid medicaments. The duties of the physician (or assistant physician) on duty are regulated by general hospital instructions.

Nurses and assistant physicians must attend only to a certain wards and their duties must be clearly defined. Each nurse is assigned to a number of wards. The wards must be equipped with light signals so that, whenever necessary, each patient may summon a nurse. Each nurse must have a locker with an assortment of medicaments, syringes with needles, sterilizers, thermometers and other objects used in the care and treatment of patients.

The head nurse of the department must supervise the work of the nurses on duty and has at her disposal a stock of medicaments and medical instruments.

A special room must be set apart for various diagnostic and therapeutic procedures. Intravenous injections, as well as lumbar and pleural punctures must be made by a physician, or assistant physician; these procedures must necessarily be recorded in the case history. For simpler manipulations (subcutaneous injections, cupping, etc.) the departments are recommended to assign a special nurse.

Grave cases, especially patients in a state of excitement, must be kept under individual observation by a nurse 24 hours a day.

The results of the daily examinations of patients, as well as the data of roentgenological, electrocardiographic and other forms of examinations, and medical consultations must be recorded in the case histories. The results of laboratory tests must be appended to the case histories.

The case histories must contain detailed information on blood transfusions (indicating how the patient endured a blood transfusion and whether or not the latter was accompanied by any side effects), the doses of therapeutic vaccines and the method by which they are administered, the series and period of efficacy of these vaccines, as well as the patient's reaction to their administration. The case histories must analogously have records of intravenous injections of certain drugs, for example, novarsenol (neoarsphenamine). The case histories must also contain the results of diagnostic tests, for example, the skin allergy tests, the therapeutic procedures administered to the patients, baths, etc.

The prescriptions and diagnostic tests entered by the physician (or assistant physician) in the case histories must be transferred by the nurse to the special prescription notebook or to the individual prescription records kept in the given division.

Upon discontinuation of the particular prescription a corresponding note must be made in the case history. The diagnosis must be recorded on the title page of the case history, and the substantiation of the diagnosis must be recorded under a corresponding date.

The district epidemiologist must be immediately notified of each new case of infectious disease by mail or messenger, as well as by phone.

The duration of the infectious patient's stay in the hospital must be determined by two factors—the degree of his clinical cure and the cessation of the period of contagiousness.

Infectious patients may be discharged from the hospital (on the basis of adequate clinical cure) only after the obligatory period of isolation. As a rule, the period of isolation of infectious patients is determined by the number of days elapsing since the moment the temperature has dropped to normal (for example, 12 days for persons surviving typhus; at the end of this period a convalescent is no longer contagious and no control check-ups on infection-carrying are made). As for convalescents surviving typhoid fever, diphtheria, epidemic meningitis and certain other diseases, the time of discharge may not be decided upon merely by the date of disappearance of the main clinical signs of the disease; to determine the absence of contagion (infection-carrying), such cases require bacteriological control. For this purpose the faeces, urine and bile taken with a duodenal probe from patients surviving typhoid fever are inoculated in a nutrient medium (see Supplement 6 for rules for discharging convalescents).

Before discharge each patient must take a bath or a shower and then must put on his own clean underwear and disinfected clothes.

Upon discharge of an infectious patient from the hospital a brief *epicrisis* must be entered in his case history. At the same time the patient must be given necessary advice concerning his regimen for 2-3 weeks.

Rules Governing the Work of the Personnel of Contagious Departments

All of the medical personnel must strictly maintain the sanitary conditions of the department and observe the rules of personal hygiene in order to avoid contracting the infection and serving as the source of infection for others. All workers of the contagious department must have individual lockers for their outer garments. The nurses, physician's assistants and hospital attendants must have, in addition to individual gowns, individual work clothes and footwear which must also be kept in individual lockers. The entire personnel must wear white cotton caps or kerchiefs which cover all of the hair and have well-trimmed nails. After examination of patients or attendance on them, involving therapeutic or diagnostic manipulations, the entire personnel of contagious hospital must disinfect the hands with a 0.5 per cent chloramine solution from a cylinder. Periodically the entire personnel must be examined for diphtheria, typhoid fever and dysentery bacteria-carrying. The entire personnel must be inoculated against typhoid fever and paratyphoids A and B. In cases of appearance of an unclear intestinal disease in some hospital worker the latter must without fail be subjected to a bacteriological test for dysentery. This test must be performed three times.

Disinfections must be carried out according to prevailing rules.

Prevention of Nosocomial (Intrahospital) Infections

Nosocomial diseases are infectious diseases which can be contracted *only* in the given department or hospital. In deciding whether the disease is really nosocomial it is necessary to take into account the duration of the incubation period typical of the given disease. For example, the incubation period of diphtheria is 2-9 days. If a child who is in a contagious department with dysentery contracts diphtheria on the 13th day of hospitalization, it is clear that he could contract diphtheria *only* while in the given department (or hospital); this is a case of nosocomial infection. In such cases it is often possible to reveal the source of infection. On the other hand, if a patient admitted to the hospital with dysentery

manifests symptoms of fauceal diphtheria about 24 hours after admission, it is clear that he contracted diphtheria before admission to the hospital, and this case cannot be regarded as one of intrahospital infections.

Proper care and observation of infectious patients, careful observance of all sanitary and hygienic rules, and placement of patients in accordance with their diseases help to avoid intrahospital infections. No nosocomial diseases must occur in contagious departments and hospitals. Each case of intrahospital infection is subject to a special discussion at conferences of the medical personnel.

The most common nosocomial infections are measles, scarlet fever, diphtheria, whooping cough, varicella, epidemic parotitis and influenza.

Prevention of intrahospital infections must begin in the admission department. While admitting a new patient, the physician or physician's assistant on duty must carefully examine the patient in order to discover signs of mixed infection and to collect an epidemiological anamnesis. The patient's contacts with infectious patients during the last 3-4 weeks preceding his admission to the hospital (this length of time corresponds to the longest incubation period of most diseases), the diseases survived by the patient and the prophylactic inoculations he was given must be ascertained. If signs of mixed infection are discovered in a patient, or if patients suspected of mixed infections, as well as patients who had contact with another infection, are admitted, they must be placed in small individual wards (or compartments). Meltzer compartments (see Fig. 9) are very convenient because they ensure the strictest isolation of patients.

Patients placed in isolation wards located within the department must be provided with individual dishes and all other things used in their care; the attending personnel must have individual gowns.

Upon appearance of nosocomial diseases in a contagious hospital or department the patients who have contracted a second infection must be immediately transferred to an isolator or a Meltzer compartment, and the department must be thoroughly disinfected.

Passive immunization against possible intrahospital infection is helpful in preventing nosocomial infections. For example, if even one child contracts measles in the department for children affected with dysentery, he must be immediately placed in an individual compartment, while all the other children in the same department must be administered human measles immune serum or gamma-globulin. If these inoculations are made, the children will either contract no measles at all or will contract a mild form of the disease.

Patients or their care by their relatives or friends in contagious departments are not allowed, except in very severe cases.

CARE AND DIET OF INFECTIOUS PATIENTS

Proper care of an infectious patient not only improves his physical and moral condition, but also helps in the quickest possible recovery and in the best restoration of his strength and working capacity. Proper care and diet are particularly important in severe infectious diseases.

The work in a contagious department must be organized so that each patient is daily ensured *a therapeutic and protective regimen*.

The nervous system participates most actively and completely in the development of the restorative reactions when the entire atmosphere of the medical institution, the care of the patient and his diet are directed toward achieving this aim.

The attention and sympathetic concern of the entire personnel of the contagious department—physicians, physician's assistants, nurses and hospital attendants—strengthen the patient's confidence in rapid recovery, promote a cheerful mood, and improve his sleep and appetite. Proper care and treatment make it possible to save the life and restore the health of patients even in the gravest and seemingly hopeless cases.

The hospital personnel must remind the patients that *a proper and calorically adequate diet constitutes one of the important means* of accelerating the process of recovery. The personnel must patiently feed grave patients.

Considerable attention must also be devoted to feeding convalescents.

Patients and convalescents must be fed at least four times a day at very definite hours.

In prescribing a diet it is necessary carefully to consider the content of the most important vitamins in the foodstuffs in view of the fact that the infectious patients need more vitamins. To enrich the diet with vitamins, such patients must be prescribed natural fruit and berry juices; in the absence of serious affections in the gastrointestinal tract the patient may be allowed fresh fruit, vegetables and berries.

In choosing dishes for patients it is necessary to consider the peculiarities of the pathogenesis and the course of the disease; for example, typhoid fever patients with intestinal ulcers require a protective diet. The patients' tastes must also, as far as possible, be taken into account.

Infectious patients often require plenty to drink which helps in the elimination of toxic and waste products from the organism. Usually, they willingly drink cranberry or black currant juices, fruit juices and tea with lemon. In cases of considerable dehydration of the organism (food toxoinfections, cholera) intravenous (preferably by the drip method) or subcutaneous injections of 0.85 per

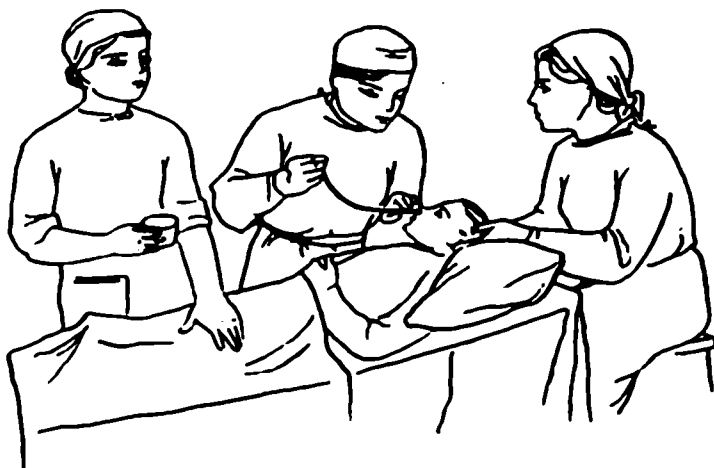


Fig. 10. Feeding through a tube in cases of diphtheritic paralysis

cent physiologic solution and 5 per cent glucose solution are administered.

In cases of deglutition disorders (dysphagia) the patients are fed through feeding tubes (Fig. 10) or are given nutritive enemas.

Considerable intoxication, extreme dehydration of the organism and difficulties in swallowing (for example, in severe cases of typhus with dysphagia, in botulism, poliomyelitis, encephalitis, smallpox accompanied by an eruption of pustules on the mucous membranes of the epiglottis) necessitate the use of *nutritive enemas*. The patient must first be given a cleansing enema and then a nutritive mixture heated to 36-37°C and consisting of milk, sugar, egg-yolk, and vitamin C must be administered from a glass funnel through a rubber catheter introduced into the rectum. A single feeding consists of 200-250 ml of the nutritive mixture; such patients must be fed 3-4 times a day. Sometimes, as in cases of disorders of deglutition, the nutritive mixture must be administered through a duodenal tube.

Children affected with diphtheritic paralyzes involving dysphagia must be fed artificial nutritive mixtures administered by means of a thin tube through the nose. With the aid of a glass funnel and a tube a child must first be given a slightly heated nutritive mixture consisting of 50 g of sugar, 50 g of butter, one egg, 200 mg of vitamin C and 150 g of milk. Owing to the danger of asphyxia in such cases the nutritive mixture should be given in the presence of two nurses ready to administer the patient first aid.

For best results of the treatment the patients must be carefully watched by the entire medical personnel of the department. The main indices of the patient's condition (pulse, respiration, stool, micturition, etc.) must be recorded by the attending physician or the physician (or physician's assistant) on duty.

Each patient's temperature must be taken twice a day (at 7 a.m. and at 6 p.m.). The thermometers used in contagious departments must be kept in a jar containing a disinfectant. In some cases, for example, in malaria, the temperature must be taken every 2-3 hours to register the attacks of fever.

Only if the patients are watched continuously, especially in cases of severe intoxication, delirium, etc., it is possible to observe sudden changes in their condition (for example, development of collapse in a typhoid fever patient), and to prevent the aggressive actions or attempts to escape from the hospital by patients with a clouded consciousness. Grave cases must be watched particularly carefully (nurses and hospital attendants must be continuously on duty).

In cases of extreme excitement patients must be administered chloral hydrate in an enema and must be placed under a special string net tied to the bed.

It should be remembered that at the end of the febrile period of some infectious diseases, for example, typhoid fever, or after the febrile period patients sometimes develop symptoms of infectious psychosis and require special observation. Various pathologic symptoms on the part of the nervous system in certain infectious diseases necessitate appropriate care and treatment of the patients.

Many infectious diseases are accompanied by general intoxication of the organism characterized by intense headaches, insomnia, bulbar disorders (disorders of speech, deglutition and movements of the tongue, choking, spasms of the muscles of deglutition, etc.) and disturbances in consciousness in the form of sopor, stupor and coma.

Some patients (for example, in cases of diphtheria) may have late paralysis of the soft palate and of accommodation. In some infectious diseases, for example, in typhoid fever and particularly often in brucellosis, affections of peripheral nerves (neuritides, plexitides, ischioradiculitides) are observed.

In cases of intractable headaches an icebag must be applied to the forehead (for 20-minute periods with 25-30-minute intervals in between). In cases of insomnia patients must be given hypnotics.

In infectious cases an important part is played by the state of the skin, since a general decrease in immunity is conducive to various purulent complications (abscesses, furuncles and pustules). It is necessary to keep every infectious patient's skin clean, to bathe such patients regularly, at least once a week; in severe cases patients must be given rub-downs with a towel soaked in warm water; the underwear and bed linen must be changed regularly and, if soiled by the patient's discharges, must be replaced immediately.

In cases of prolonged infectious diseases accompanied by considerable emaciation, the patient may develop bed sores which may serve as portals of entry for secondary infection often resulting in

streptococcal or staphylococcal sepsis. This danger threatens particularly typhus and typhoid fever patients. The medical personnel must not overlook the possibility of *trophic* skin lesions connected with neurotrophic disturbances in skin nutrition, for example, in severe cases of typhus. In such cases trophic ulcers developing as a result of nutritional disturbances in soft tissues may appear not only at sites of greatest pressure on the skin (sacrum, buttocks, angles of scapulae), but also outside these areas, for example, on the anterior surface of the thighs.

To prevent development of bed sores, it is necessary to apply vegetable oil to the skin at the sites of greatest pressure, turn grave patients over in bed more frequently, and, if necessary, place rubber rings under them.

In watching the activity of the respiratory organs it is necessary to devote special attention to the respiratory rate, the general character of respiration and its pathology (Cheyne-Stokes respiration, Biot's respiration, stenotic respiration, etc.), coughing and discharge of sputum, its amount and appearance (colour, consistency, etc.). The foregoing pathologic symptoms on the part of the respiratory organs are characteristic of some infectious cases in severe forms of intoxication, coma, various neuroinfections (rabies, spring-summer encephalitides) and pneumoniae.

Stenotic respiration is observed in diphtheritic croup; stertorous respiration occurs in pulmonary oedema.

The patients' sputum must be collected in separate utensils with tightly closing lids and disinfected with a 3 per cent lysol solution. For laboratory analyses the sputum must be collected in glass jars, washed in boiling water and covered with lids.

Long confinement of infectious patients to bed, especially in cases of prolonged pathology, is conducive to development of *hypostatic pneumonia*. To avoid this, such patients should be more frequently turned over in bed.

The pathologic process of various infectious diseases often involves the cardiovascular system. It is therefore necessary to watch the patient's pulse (rate, tension, filling, rhythm, diastole), to check on the patient's blood pressure more frequently, examine the percussion borders of the heart and note the auscultative data (sounds, their splitting and the character of murmurs).

In the treatment of infectious patients, especially in acute intestinal diseases, it is important to watch the activity of the gastrointestinal tract; no small part is played by proper care and regular feeding of the patients, as well as prevention of possible digestive complications.

It is first of all necessary to watch the oral cavity. Every patient must rinse his mouth with warm water after each meal and brush his teeth regularly. A nurse or physician's assistant must carefully swab 2-3 times a day the mouth of each patient with a cotton tam-

pon soaked in a 2 per cent boric acid solution; this must be done cautiously to avoid injuring the mucous membrane. The patient's tongue must be cleaned by a similar method. If the patient's tongue is dry, it should be moistened with a half-and-half mixture of glycerin and water. The cracks in the tongue must be painted with a 2 per cent silver nitrate solution. Regular cleaning of the oral cavity helps to prevent purulent parotitides which may develop, for example, in typhoid fever and typhus as a result of ascending infection penetrating into the tissue of the parotid gland through the parotid duct.

Some infectious diseases, for example, typhoid fever, are accompanied by constipation and meteorism.

In cases of constipation the patient must be given cleansing enemas consisting of 3-4 glassfuls (for adults) of cool water (33-34° C). The enema must be administered from a rubber bag or from Es-march's can.

In cases of particularly persistent constipation the patient must be given a hypertonic enema (250 ml of a 10 per cent common salt solution).

In cases of strongly pronounced meteorism a colonic tube must be used.

Infectious patients must be given individual bedpans.

In cases of vomiting patients must be turned on a side, head lowered, so that the vomitus may not gain entrance into the respiratory tract and cause aspiration pneumonia. Vomiting is often arrested by swallowing small pieces of ice or intake of a peppermint mixture (8-10 drops per half a glassful of cool water).

In view of possible collapse in cases of typhoid fever and paratyphoids A and B such patients must defaecate into bedpans; they must not be allowed to rise and defaecate, nor to sit up in bed before the 5-8th day of normal temperature.

The urine must be analysed every day in all cases of infectious diseases. Sometimes it is necessary to measure the daily output of urine and the amount of liquid consumed (to determine the water balance).

The course of various infectious diseases, especially of typhoid fever, may become complicated by inflammation of the renal pelvis and the urinary bladder, most commonly involving development of catarrhal processes (pyelitides and pyelocystitides). In such cases patients must be prescribed appropriate treatment (penicillin, synthomycin, biomycin), a dairy and vegetable diet and plenty of alkaline mineral water. If necessary, especially if sepsis is suspected, urological and gynaecological examinations must be made.

Certain therapeutic and diagnostic manipulations must be performed only by a physician or a physician's assistant. These manipulations include, in particular, intravenous injections of various medicinal substances, lumbar and pleural punctures, blood trans-

fusions, abdominal punctures in cases of ascites, catheterization of the urinary bladder, and diagnostic skin tests (Burnet's test, tularin test, etc.). Some therapeutic and diagnostic manipulations must be performed directly at the patient's bedside, others, requiring appropriate surroundings—in special rooms. Such manipulations, particularly the technique of blood transfusion, should be taught to one or two nurses to whom, if necessary, their performance may be assigned.

Subcutaneous and intramuscular injections, catheterization, cupping, administration of enemas and application of compresses must be performed by physician's assistants and nurses working in the departments.

All diagnostic and therapeutic manipulations must be performed under conditions of strict asepsis and antisepsis; this is particularly necessary in cases of infectious patients whose lowered resistance makes them susceptible to secondary, mainly purulent infection.

It should always be remembered that the problem of recovery from infectious diseases is solved not only by proper treatment, but also by considerate and skillful care of the patients; this also applies to prevention of intrahospital infections.

PRINCIPAL METHODS OF TREATING INFECTIOUS PATIENTS

The modern clinic has a number of medicinal substances, vaccines, serums and bacteriophages which make possible effective treatment of infectious patients. In recent years medicine has acquired a number of new preparations—antibiotics—which are successfully used in therapeutic practice.

Until the beginning of the 19th century the use of ipecac for the treatment of amoebiasis, and of a decoction of the cinchona bark for the treatment of malaria rested on purely empirical grounds.

Quinine (alkaloid) which is the active principle of the cinchona bark was synthesized in 1821; this laid down the foundation for substantiated *chemotherapy* of infectious diseases.

In the beginning of the current century therapeutic practice started utilizing arsenicals (salvarsan, neosalvarsan) which proved very effective in the treatment of relapsing fever, syphilis and anthrax. Streptocido and sulphidine (sulphapyridine) were synthesized in the 1930's; other sulphanilamide preparations were developed somewhat later. The era of antibiotics began in 1941 when penicillin was used for the first time in the treatment of infections caused by cocci. During the years that followed many new antibiotics were produced—streptomycin, synthomycin (chloramphenicol), levomycetin, tetracycline, biomycin (chlortetracycline), etc. The antibiotics in-

clude quite a number of synthetic medicinal substances, particularly synthomycin and levomycetin.

The progress of chemotherapeutic research increasingly extends the possibilities of active interference in the development of the infectious process and of achieving a rapid cure in many, often very grave cases. Treatment with antibiotics almost completely prevents death from typhoid fever, typhus and other infectious diseases. Large doses of streptomycin have made it possible to treat such severe diseases as tuberculous meningitis and pulmonary plague. Penicillin is effectively used in the treatment of patients affected with epidemic meningitis, relapsing fever and leptospiroses. Synthomycin and levomycetin are effective agents in the treatment of typhoid fever and typhus. Typhus and dysentery have been successfully treated with biomycin. Tetracycline and terramycin are used in various infectious diseases; these preparations, closely allied to biomycin, less frequently produce side effects. Children affected with colienteritides are extensively administered colimycin and mycerin. Erythromycin whose spectrum of action coincides with that of penicillin is a very potent antibiotic.

A medicinal substance administered to a patient must exert vigorous action on the causative agent of an infectious disease in the organism; this is the first and most important principle of rational chemotherapy. The brilliant successes of antibiotic therapy are due primarily to the *specific* influence of the antibiotics on the causative agents of infectious diseases. Of course, this specificity does not exclude the possible influence of one preparation on a number of pathogenic microbes or protozoans, which is the case with many antibiotics of a "broad spectrum of action" (streptomycin, biomycin and a number of other preparations).

Several examples may be cited to confirm that various preparations possess an exclusively high specificity of action which determines their ability to influence only certain stages in the development of the causative agent of an infectious disease. For example, the action of acrichine (quinacrine), plasmocide (pamaquine naphthoate), bigumal (paludrine) and quinocide (antimalarial aminoquinoline derivative) depends on the biological cycle of the causative agent of malaria.

The specific mechanisms of the influence exerted by drugs on the causative agents of infectious diseases must be regarded as based on the special features of microbial metabolism. By acting on the microbial cell drugs and antibiotics suppress and block their enzymatic systems with the result that they produce a bacteriostatic effect, i.e., arrest the multiplication of microbes.

The action of drugs, sulphonamides in the first place, is in large measure determined by the similarity of their chemical structure with the substances that play the leading role in the metabolic processes of the bacteria which are sensitive to the particular drug. For example, streptocide and paraaminobenzoic acid, in addition to considerable similarity of their chemical structure, are competitors in the metabolic processes of the dysentery bacillus, the streptococcus and the meningococcus. In acting on the bacteria which are sensitive to it streptocide imitates paraaminobenzoic acid, which is necessary for the normal life of these microbes, with the result that their enzymatic system is blocked and becomes incapable of performing normal metabolic functions.

In a number of cases the specific action of drugs and antibiotics is limited to their predominant influence only on individual aspects of the life of micro-

bial cells. For example, penicillin exerts an influence on the bacteria which are sensitive to it mainly at the stage of their division, whereas levomycetin and biomycin usually suppress this stage of development of microorganisms.

Drugs act in the organism of an infectious patient not only through their direct influence on the metabolism of the causative agent of the disease but also because the organism itself helps the drugs to influence the microbes. The thing is that in the patient's organism drugs and antibiotics are subjected to certain chemical and physico-colloid action of various biological substrates (blood, lymph, tissue fluid, transudates and exudates, cerebrospinal fluid and cell protoplasm in various organs and tissues). The products of transformation of the drugs, in addition to their direct action in their main chemical form on the microbial cell, block the enzymatic system of the microbes. It is well known, for example, that the change of pentavalent arsonic to trivalent arsonic in the human organism is alone able to produce the chemotherapeutic effect of nov-arsenol in recurrent spirochaetosis. The metabolism of the microbe also changes in the patient's organism.

Such are the main features of the etiotropic influence exerted by drugs on the pathogenic microbes in the organism of an infectious patient. It should be emphasized that under these conditions a chemotherapeutic effect may be produced even with comparatively small concentrations of the medicinal substances contained in the blood or other biological fluids of the organism, but the *optimum* effect is achieved only with sufficiently high therapeutic concentrations of these drugs in the blood. It is therefore necessary that antibiotics and drugs should be administered in sufficiently large single doses and at such intervals which ensure the necessary constancy of therapeutic concentrations of the given preparation in the blood.

It follows that one of the main principles of rational administration of antibiotics and drugs in infectious diseases is, in addition to the factor of their specific action on the causative agent of the disease, the principle of choosing *adequate doses* and observing the necessary *intervals* between the intakes of the medicinal substance. The intervals between the individual intakes of drugs depend on the speed with which they are absorbed in the intestines and with which they are eliminated from the organism. For example, owing to the slow absorption in the intestines and similarly slow elimination from the organism, it is enough to administer biomycin only four times a day, whereas levomycetin, which is eliminated from the organism comparatively rapidly, should be prescribed to be taken at shorter intervals (six times per day).

In addition to the foregoing factors, an important role is played by the *duration* of the therapeutic course and *its continuity*. In cases where infectious patients are given a very short or intermittent (two-stage) course of treatment the therapeutic effect often proves entirely inadequate. A. N. Filippovich's observations of two analogous groups of typhoid fever patients of which one group was given a prolonged and continuous course of synthomycin treatment and the other a two-stage course of treatment may serve as a good illustration of the superiority of a continuous course of treatment of typhoid fever patients with synthomycin (or levomycetin). The aforesaid author established that a drop in temperature and the elimination of other pathological symptoms by a two-stage method of treatment are considerably retarded and that relapses of the disease occur twice as often as they do in a continuous course of treatment up to the 10th day of normal temperature. Interruptions in the treatment undoubtedly delay the restoration of normal anatomical structures impaired by the infectious disease (as was shown with regard to specific granulomas in typhus).

Of course, the aforesaid does not in any way depreciate the importance of repeated therapeutic courses (cyclic treatment) in infectious diseases which tend to a protracted and even chronic course (brucellosis, dysentery, malaria, amoebiasis); at any rate, administration of antibiotics and drugs must not be suspended immediately after weakening of the main symptoms of the disease or after normalization of the temperature.

An important principle of rational chemotherapy, as well as treatment with antibiotics, is the *earliest possible institution* of specific treatment. This emphasizes the enormous importance of early diagnosis. Attempts should be made to begin treatment before stable and sometimes scarcely reversible anatomical changes have developed in the patient's organs and tissues. Observations have shown that in the treatment of typhoid fever, typhus and dysentery patients with antibiotics the pathomorphological pictures of these diseases retain their clinical importance, although they are subject to partial changes.

An exceptionally important role in the effectiveness of treating infectious patients with antibiotics and drugs is played by the state of the organism's *immunological reactivity*. A number of observations conducted in our clinic in recent years have shown that a long-enough continuous course of treatment with antibiotics (synthomycin, levomycesin, biomycesin, tetracycline) using medium therapeutic doses causes no essential changes in the usual dynamics of forming immune reactions of the organism in typhoid fever and dysentery. A certain inhibition of immunological reactions depending on a decrease in the mass of the antigenic stimulus and on the toxic effects of the preparation may occur only in cases of very early administration of antibiotics.

Entering the human organism sulpha drugs and antibiotics exert certain pharmacodynamic influences on it. It has been shown that in the human organism many sulpha drugs, for example norsulphazol (sulphathiazole), and antibiotics (biomycesin) are fixed by the plasma proteins; this circumstance not infrequently reduces the therapeutic effect of the preparation and unfavourably affects its diffusion directly into the focus of infection (into the specific granuloma, parenchymatous organs, pleural exudate, etc.). Owing to this, antibiotics are administered, when indicated, *directly into the focus of affection* or near it; for example, in epidemic meningococcal meningitis, in addition to intramuscular administration of penicillin, small doses of crystalline sodium penicillin are administered endolumbarly, while in tuberculous meningitis a calcium chloride complex of streptomycin is administered endolumbarly and suboccipitally. However, considering the possibility of very rapid disintegration of microbes and the injurious effect of the antibiotic on the tissues, this method must be used with great caution.

The bacteriostatic effect produced by antibiotics in the infectious patient's organism allows various factors of immunity to develop, which in the end overcome the infectious process in the organism. At the same time, in a number of cases (for example, in the treatment of typhoid fever patients), the antibiotics (synthomycin, levomycesin) do not diminish the frequency of resultant bacteria-carrying.

In the process of antibiotic treatment a number of cases show development of resistance of the causative agents to the antibiotic. In diseases caused by the *coccal flora* (purulent meningitides, pneumoniae, etc.) the development of the causative agents' resistance to the antibiotics considerably *reduces* the therapeutic effect of these preparations. The resistance of the causative agents may play a certain role in the treatment of patients affected with dysentery, whooping cough and certain other diseases; however, these diseases are few and in many infectious diseases the study of the resistance of microbes to medicinal preparation is of no practical importance.

It should be remembered that in a number of cases, as, for example, in dysentery, no direct parallelism between the extent of the microbes' resistance to medicinal substances and the therapeutic effect of the antibiotic being administered is observed. All strains of typhoid fever bacteria isolated from the patients today are sensitive to antibiotics. The existing methods of determining the degree of resistance of microbes to antibiotics far from completely reflect their actual sensitivity in the organism. The most efficient of the suggested methods are the method of serial dilutions and the three-disk method. The clinical and other indices of the effectiveness of the treatment must be carefully considered in all cases.

A particularly potent therapeutic effect is ensured by combined administration of antibiotics. This constitutes one of the important principles of rational therapy of infectious patients. However, in choosing antibiotics for their combined administration it is necessary to take into consideration their competitive or synergistic relations arising in the organism. For example, penicillin and streptomycin are constant synergists and may be effectively used in severe cases of acute infectious diseases (in pneumoniae, various purulent complications and mixed infections).

It must also be taken into consideration that in combined treatment with two different antibiotics the resistance of the causative agents to each of the antibiotics being used may develop much less frequently and more slowly than when only one of these antibiotics is administered. Nor must we ignore the fact, however, that combined treatment with antibiotics increases the frequency of undesirable side effects which complicate medicinal therapy; these questions are treated in greater detail below, as is also the question of the expedience of successively changing from the administration of one antibiotic to that of another in the course of treatment. This scheme of treatment may be used, for example, according to the instructions concerning early discharge of dysentery patients and their subsequent treatment at home.

While antibiotics and various drugs are potent agents in the treatment of infectious patients, they must not be regarded, however, as self-dependent methods of treatment and should not be used outside the complex of all therapeutic measures carried out at the patient's bedside. The truth of this proposition is substantiated by many facts of clinical practice showing that *only overall* therapy using modern methods of treatment may ensure its high effectiveness.

Considerable importance has of late been attached to the role of vitamins and hormones (cortisone, prednisone, prednisolone) in overall therapy of infectious patients. The questions of vitamins and hormones are now decided in the following manner. Saturation of the patient's organism with large doses of ascorbic acid (vitamin C) is necessary in all infectious diseases; other vitamins must be prescribed strictly according to indications. It is also very important to administer the complex B vitamins.

Cortisone, prednisone and prednisolone are indicated only in cases of increased sensitivity of the organism and extreme toxicosis: in bacteriaemia infectious diseases accompanied by formation of tissue foci (brucellosis) these hormones may cause the infective agents to break out of the foci and produce extreme septicemia by suppressing the inflammatory reaction in the foci. It is necessary to control the potassium level in the blood and to determine the 17-ketosteroids.

Special emphasis must be laid on the fact that, owing to the cyclic course of a number of infectious diseases, the effectiveness and the very character of the therapeutic measures may essentially change depending on the period of the disease. In this respect it will do well to take into consideration the practice of treating brucellosis patients; whereas during the acute period of the disease, which is characterized by generalization of the infection, treatment mainly with antibiotics (biomycin, levomycetin) is indicated; in subchronic and chronic forms of brucellosis the main part of the treatment

consists of vaccine therapy combined with blood transfusion, physiotherapeutic and balneological procedures, and vitamin therapy.

The main effect produced by antibiotics is *bacteriostatic*, whereas the infectious process is finally terminated owing to the development of natural defence factors of the organism—agglutinins, lysins, precipitins, phagocytic activity of the leucocytes and other factors of immunity.

The use of antibiotics and drugs essentially changes the clinical picture of an infectious disease.

It has been shown that, when *usual therapeutic doses* are administered in a continuous but strictly limited course of treatment, antibiotics exert no inhibitory influence on the development of the immune reactions of the organism. It goes without saying that in the treatment with antibiotics the factors of immunity play a serious role in the success of the therapy. It is extraordinarily important to administer antibiotics in adequate single and daily doses not only during the febrile period, but also for several days after the drop in temperature (for example, in typhoid fever synthomycin is administered until the 10th day of normal temperature). Moreover, antibiotics must be administered several times a day to ensure their therapeutic concentration in the patient's blood; in some cases, to achieve the foregoing aims, the patient must be given antibiotics even at night.

Many antibiotics are administered only per os (synthomycin, biomycin, levomycetin), others—both per os and parenterally (streptomycin and tetracycline may also be administered intramuscularly).

Various penicillin salts (sodium, potassium, calcium) may be administered intramuscularly (Fig. 11), but only the sodium salt



Fig. 11. Intramuscular administration of a penicillin solution

of purified crystalline penicillin is fit for endolumbar administration.

Some antibiotics are used only externally; for example, a 0.04 per cent warm gramicidin solution is used (in enemas) for the treatment of ulcers in the rectum and sigmoid colon of dysentery patients. The activity of an antibiotic and its therapeutic dose are measured either by the number of units of action (streptomycin, penicillin) or by weight (synthomycin, levomycetin, biomycin). There are certain correlations between the number of units and the weight of biomycin and streptomycin; 1 g of each of these antibiotics contains 1,000,000 U.

The readily soluble and hardly soluble sulpha drugs (norsulphazol [sulphathiazole], disulphormin [1,4,4'-N-trimethylene-bis-(sulphanilyl-sulphanilamide)], phthalazole [phthalylsulphathiazole], sulgine [sulphanilylguanidine], sodium ethasole [2-(para-aminobenzolsulphamido)-2-ethyl-3,4-thiodiazole]) which are used in the treatment of dysentery and erisypelas have not lost their validity. Novarsenol is used in the treatment of anthrax and relapsing fever. Antimony preparations (mainly solusurmine [sodium salt of complex pentavalent antimony compound with gluconic acid]) are used in the treatment of visceral leishmaniasis, and emetine, aminarsone (carbasone) and yatren—in the treatment of amoebiasis.

The superiority of chemotherapeutic preparations, as effective agents in the treatment of infectious diseases, is perfectly obvious. It must not be forgotten, however, that individual patients who have increased sensitivity to these preparations may sometimes exhibit very strongly pronounced toxicallergic manifestations known as drug pathology or drug diseases. The signs of drug pathology may be nausea, vomiting, development of stomatitis and thrush, diarrhoea (the stool may sometimes contain mucus), urticarial eruption on the skin, hypotension, elevated temperature, etc. Overdosing of the preparations, as also their unnecessarily prolonged and irregular administration, may lead to grave results.

In cases of particularly intense toxic and allergic reactions treatment with a particular antibiotic (synthomycin, biomycin) has to be suspended; however, in many patients the already developed toxic and allergic phenomena disappear without leaving a trace despite the continued treatment with antibiotics. Antibiotics are capable of partly suppressing the normal flora of the digestive tract, including the antagonists of pathogenic bacteria, thereby causing dysbacteriosis. As the result, the patients given antibiotics may develop a febrile reaction and, sometimes, severe mycotic affections (candidids) of a septic character.

Although the manifestations of drug pathology developing during the treatment with various antibiotics have a good deal in common, their frequency varies with the properties of the particular antibiotic. For example, biomycin and streptomycin are more

toxic than penicillin which is well tolerated by most people. In some cases streptomycin causes severe affections of the vestibular apparatus and the acoustic nerve. But even so hardly toxic an antibiotic as penicillin may cause phenomena of drug pathology in individual patients. The development of side effects is in large measure determined by the patient's individual sensitivity to the given antibiotic. We have already mentioned that in infectious diseases caused by the coccal flora there is a rather clear interdependence between the resistance of the microbes to antibiotics and the therapeutic effects of their administration. In dysentery patients treated with antibiotics no such parallelism is observed, which may be due to the favourable effects produced by antibiotics through a decrease in toxicosis and a suppression of the antagonistic flora.

Antibiotics and sulpha drugs may in a number of cases be combined in order to strengthen their mutual action—synergistic effect; for example, synthomycin and sulgine are prescribed in the treatment of acute dysentery.

Vaccines—specially prepared killed cultures of the causative agent of a given disease—are also used in the treatment of infectious patients. Vaccine therapy is resorted to mainly in the treatment of brucellosis and chronic dysentery. Vaccines are administered intracutaneously, subcutaneously and intravenously. The last method is employed very cautiously because it may be accompanied by extreme reactions manifested in a considerable rise in temperature, vomiting and a drop in blood pressure. The dose of a vaccine is measured by the number of microbial bodies. The injections are repeated at certain intervals, the single dose being gradually increased.

Vaccine therapy has found wide application in chronic dysentery, as well as in subacute and chronic brucellosis (see chapters dealing with these diseases).

Whatever the method of administration, a vaccine serves as a stimulus of specific sensory nerve endings and acts at the site of administration, and, after absorption, on the nerve endings of the sensory nerves in the walls of the blood vessels, in various tissues and organs. This is accompanied by an allergic reorganization of the organism and complex neuroreflex influences on the entire organism, which contribute to enhancement of all the defence physiologic functions and to overcoming of the infectious process. Nor can it be doubted that the vaccine which contains specific antigens activates production of antibodies and phagocytosis by acting directly on the reticuloendothelial system.

The specific resistance of the organism to the causative agent of the given disease considerably increases and its immune reactivity is reorganized in a desirable direction.

An important part in the treatment of many infectious patients is played by *serums*.

The therapeutic administration of the diphtheria antitoxic serum produced by Behring and Roux in 1894 proved sufficiently effective and laid down the foundation for serum therapy which has since then saved numerous lives of diphtheria patients in many different countries. The production of the antidiphtheritic serum was followed by production and introduction into medical practice of antitetanic, scarlet fever, antibotulinus and other therapeutic serums which are still valid today.

Most therapeutic serums are *antitoxic*. They include the antibotulinus, antidysenteric (Grigoryev-Shiga), scarlet fever, antitetanic and antidiphtheritic serums. As a rule, antitoxic therapeutic serums are prepared for the treatment of infectious diseases whose causative agents form *exotoxins*. These serums are produced by immunization of horses with the exotoxins of the causative agents of a number of diseases, the particular exotoxin being obtained by cultivation of the corresponding pathogenic bacteria (for example, diphtheritic, tetanic, etc.) in broth; anatoxin is most commonly used to immunize horses.

Antimicrobial serums constitute a special variety of therapeutic serums; they are prepared by immunization of horses with a pure culture of the corresponding causative agents, i.e., the direct microbial antigen or its polysaccharide complexes obtained in pure form. Antimicrobial serums include, in particular, the antianthrax, antiplague and a number of other therapeutic serums.

Since the introduction of sulpha drugs and antibiotics into medical practice, many microbial serums have lost their therapeutic importance (as is, for example, the case with antipneumococcic serum used for the treatment of croupous pneumonia until 1940). Other serums, for example, the antianthrax antibacterial serum, now play the role of auxiliary therapeutic agents used in addition to antibiotics.

At the same time research in antimicrobial serums has of late been extended and the serums have been increasingly used in the treatment of infectious diseases whose causative agents belong to the group of filtrable viruses; such, for example, are the antisera used for the treatment of influenza, tick-borne spring-summer encephalitis and other infectious diseases. To be sure, the therapeutic effect of these serums does not as yet quite satisfy the clinical requirements, but continued research and practical studies of antiviral serums are absolutely necessary, especially since modern medicine does not as yet have medicinal substances effective in virus infections.

It cannot be doubted that the use of immune gamma-globulins which replace serums has a great future.

These biological substances are prepared by hyperimmunization of horses with a corresponding toxin, anatoxin or pure culture of the causative agent of the disease. Immune gamma-globulins are

now widely used in the treatment of a number of so-called children's infections (measles, varicella, whooping cough). In addition to the usual preventive inoculations against rabies with Fermi's or Phillips' vaccines, a person bitten or salivated by a rabid animal (after a period of not longer than 14 days) is now simultaneously administered immune antirabic gamma-globulin. By such administration this preparation becomes an agent of preventive, early treatment which is particularly important in cases of severe bites by rabid animals on the face, head or neck.

As for anti-exotoxigenic serums, despite the wide use of various antibiotics and various other chemotherapeutic agents in infectious diseases, they have completely retained their role as *the main agents* for treating certain infectious diseases—botulism, diphtheria and tetanus. In addition to this, antitoxigenic serums are successfully used as agents which help to eliminate the toxic manifestations of diseases treated with antibiotics (toxic cases of acute dysentery caused by Grigoryev-Shiga bacteria, and toxic forms of scarlet fever). All doses of antitoxigenic serums are expressed in antitoxigenic units (AU). The measure for antibacterial serums is the number of units of their volume, because the activity of a serum is in these cases determined by the standard conditions of immunizing horses with a microbial culture with subsequent strictly established technological methods of purification and concentration of the serum; the amount of serum administered, for example, in cases of plague is 150-200 ml.

The general principle for using all therapeutic serums is to start treatment as soon as possible, which makes it incumbent upon the physician to establish a correct diagnosis at *the earliest possible period* of the infectious disease. The highest therapeutic dose of serum must be given the patient in the first administration and may be somewhat reduced on subsequent days. The reason for it is that the serum and the toxin interact best (in the sense of neutralizing the microbial poisons) during the first administration, whereas repeated administrations of serum cause formation of precipitins in the organism, which block the serum (both antitoxigenic and antibacterial) and diminish its therapeutic effect.

Serum may be administered subcutaneously or intramuscularly. Before administration the serum must be heated to 58°C and then cooled to 30-35°C. The number of antitoxigenic units per one ml of serum is indicated on the ampule label. Serum must be stored at a temperature of 4°C in a dry and dark place.

As was already mentioned, in rare cases administration of serum may produce an anaphylactic shock. To avoid this dangerous complication, serum is administered by Besredka's method, i.e., a small amount of serum (0.5 ml) is administered intramuscularly or subcutaneously and the rest of it is administered later—within 1-1.5 hours. Of late Besredka's method is being gradually replaced by a

more reliable and simpler method of *fractional* serum administration, i.e., 0.1 ml of serum is administered subcutaneously first, 0.2 ml is administered 30 minutes later, and the rest of the serum prescribed for the patient is administered intramuscularly one hour later. However, the simpler Besredka's method, mentioned above, may also be used.

Treatment of patients with serums may sometimes lead to *serum sickness*, i.e., a special reaction of the patient's organism to administration of foreign serum protein. Two or three days, but most commonly 8 to 12 days after the first administration of the serum patients react with a rise in temperature, general indisposition, dizziness and nausea; in these cases the arterial pressure drops and the skin develops an abundant and very itchy eruption in the form of irregular stellate lesions elevated above the skin and resembling nettle rash. Often the joints swell and the regional lymph nodes (closest to the point of serum administration) enlarge.

Serum sickness may considerably complicate the course of the main disease. The use of well-purified serums prepared by the method of fermentation decreases the possibilities for development of serum sickness. This makes it possible to remove from the serum all the reactogenic (ballast) proteins, which is very important for clinical practice.

Antibacterial serums are a special type of serum from time to time used in the treatment of infectious patients. The antianthrax serum administered in doses measured in volumetric units (ml) may serve as an example. Immune gamma-globulins are coming to be increasingly more widely used.

In some infectious diseases a specific bacteriophage is administered per os mainly as an auxiliary therapeutic agent; for example, in cases of cholera, bacteriophage is given per os in a dose of 30-40 ml twice a day (between meals), each intake of the phage being drunk down with a glassful of a warm 2 per cent bicarbonate of soda solution.

Fractional blood transfusions (125-150 ml) at 3-4-day intervals are recommended for the purpose of enhancing the general resistance of the organism in protracted infectious diseases (brucellosis, chronic dysentery).

Physiotherapy also finds application in the treatment of infectious patients; it is particularly widely used in cases of motor dysfunction (brucellosis, acute poliomyelitis); it includes applications of curative muds, ozocerite, galvanic and faradic currents and diathermy.

An adequate, vitamin-rich diet with due regard for the pathogenic peculiarities and the stage of the infectious disease must contribute to the success of the treatment.

DISINFECTION, DISINSECTION AND DERATIZATION

In the broad sense of the word *disinfection* implies eradication or elimination of the infectious element (pathogenic microbes which are the causative agents of various diseases). At the same time disinfection is divided into three forms of controlling the spread of infectious diseases: (a) disinfection proper—extermination of pathogenic microbes; (b) disinsection—extermination of insects and arthropods as vectors of infectious diseases; and (c) deratization—extermination of rodents (rats, mice, etc.) which are carriers of a number of infectious diseases.

One of the methods of sanating communities is regular *prophylactic* disinfection regardless of whether or not there are any infectious diseases at the time. For example, water is boiled and chlorinated and milk is pasteurized for the purpose of preventing intestinal infections.

Current disinfection is carried out in the immediate surroundings of patients; this includes systematic cleaning of the premises and detoxication of the patient's excrements. It is very important that the attending personnel should strictly observe the rules of personal hygiene. Since all infectious patients are hospitalized, current disinfection is carried out mainly in hospitals.

The *final* disinfection takes place in the patients' homes after their hospitalization. This type of disinfection is also carried out in the hospital upon discharge of a convalescent or the death of a patient. It is necessary to emphasize the importance of timely disinfection.

Disinfection is carried out mainly by physical and chemical methods.

Direct sunlight and desiccation destroy many pathogenic microbes. By mechanical cleaning (scrubbing the hands with hot water and soap, moist sweeping of the floor, laundering the linen, etc.) we help to remove a considerable part of pathogenic microbes together with the dirt and dust.

Good results are produced by heat. Boiling is a reliable method of disinfection: dishes, bedpans, spittoons, surgical instruments, brushes, etc., are sterilized in boiling water.

Autoclaves (special apparatus in which the temperature of the steam may reach 120 C because of elevated pressure) are used to destroy the spores of microbes (for example, the spores of *Bacillus anthracis*).

Ultraviolet irradiation by means of mercury quartz lamps disinfects the air in the patients' homes and in hospital wards.

By means of chemical disinfectants (at a certain concentration of their solutions and period of their action) it is possible to destroy causative agents of diseases.

Chemical substances are used to disinfect patients' excrements, cesspools, the soil, etc.

The surfaces of objects are disinfected by spraying with solutions of chemical disinfectants.

Disinfection chambers are widely used to disinfect outer garments, bedding, textiles, furniture, books and other objects.

There are many types of disinfection chambers which differ in structure and in the character of disinfection. Each chamber consists of a chamber proper in which the things to be disinfected are placed, sources of heat (steam boiler, fire burner) and control and measuring instruments. Some types of chambers make possible the use of chemical disinfectants (for example, formalin) and the removal of air.

There are stationary chambers (in the hospitals, disinfection stations, and delousing stations) and portable chambers. Figures 12 and 13 show delousing stations with installations for disinfection.

FUNDAMENTALS OF INFECTIOUS DISEASE PREVENTION

The planned nature of the Soviet public health services, utilization of all achievements of advanced science, extensive prophylactic measures, availability of medical aid, hospitalization with free treatment, care and feeding of patients, combined with a steady rise in the material and cultural standards of the people have made it possible completely to eradicate a number of infectious diseases, to reduce the spread of many other infectious diseases and to try to eradicate all infection.

Such diseases as smallpox, plague, cholera, dracunculosis and malaria, recurrent fever and typhus have been completely wiped out in the Soviet Union.

At the same time we must not overlook the danger of infectious diseases which may be brought in from other countries and of the natural foci of some infectious diseases (pappataci fever, leishmaniasis, seasonal encephalitides, tick-borne typhus, tularaemia, etc.); this necessitates systematic adoption of extensive prophylactic measures.

The foregoing offers a good idea of the enormous role played in Soviet public health by the system of preventing infectious diseases, which is aimed at reducing their incidence and finally eradicating them.

An important role in the epidemic services of the USSR is played by numerous sanitation and epidemiological centres which include sanitation, epidemiological, disinfection, malariological, helminthological and other departments. The complex and planned nature of the measures, scientific approach to the solution of urgent public

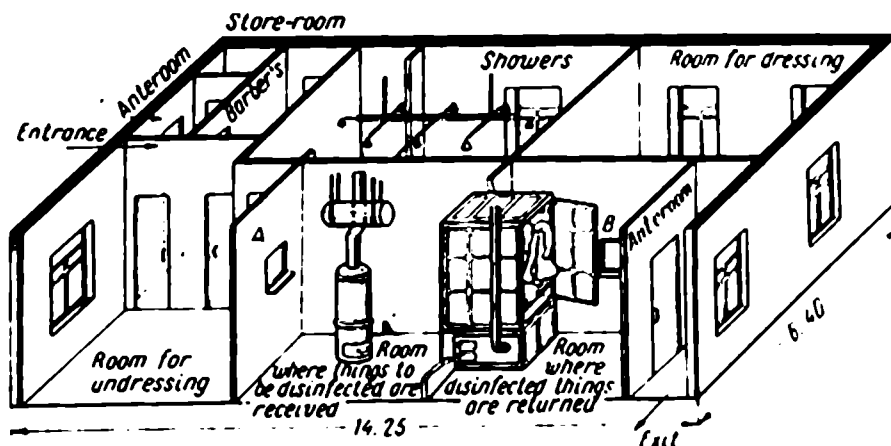


Fig. 12. Rural house adapted for a delousing station

A—window for passage of clothing and linens to be disinfected; B—window for passage of disinfected clothing and linens

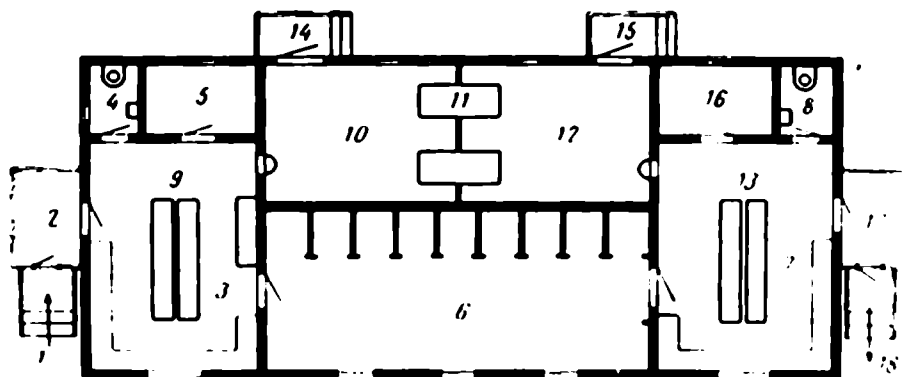


Fig. 13. Bath-house and delousing station with disinsection chambers

1—entrance; 2—lobby; 3—room for undressing; 4—toilet adjoining the room for undressing; 5—barber's; 6—showers; 7—room for dressing; 8—toilet adjoining the room for dressing; 9—window for passage of things to be disinfected; 10—room where things to be disinfected are loaded into disinsection chambers; 11—disinsection chambers; 12—room where disinfected things are unloaded from disinsection chambers; 13—window for passage of disinfected things; 14 and 15—service entrance and exit; 16—service room; 17—lobby; 18—exit

health problems, extensive connections with the sanitation services (at industrial enterprises and offices, on state and collective farms, and with the Union of the Red Cross and Red Crescent Societies of the USSR), health education work and development of hygienic habits among the population are some of the most important aspects of the work of the sanitation and epidemiological centres. A very important part is played by public sanitary inspectors.

In addition to the sanitation and epidemiological centres some Soviet communities also have specialized establishments, namely, antiplague centres, helminthological centres, intestinal infection centres, etc. These establishments control various infectious diseases; they discover infectious patients and keep records of them, administer out-patient treatment, keep these patients under observation, carry out preventive measures by means of inoculations and various drugs, discover and control epizootics, etc.

The character of anti-epidemic measures depends on the local conditions under which the infectious diseases spread, the prevalent routes of transmission operating at the given moment, the degree of susceptibility of the population, and other factors. For example, if there is any danger of smallpox being brought into the given area, the entire population must be given preventive inoculations regardless of preceding vaccinations and revaccinations.

The following are the most important methods of controlling infectious diseases:

- (1) discovery of the sources of infection;
- (2) hospitalization of patients;
- (3) blocking the routes of transmission of the infection;
- (4) reduction of the susceptibility of healthy people (preventive inoculations).

The source of infection with most infectious diseases is the diseased person or bacteria carrier. However, there is a group of infectious diseases—zoonotic diseases—which first attack animals and are transmitted from them to man; in these cases the diseased person may be barely contagious or not contagious at all (brucellosis, tularemia).

Bacteria can as the causative agents of a disease persist in the human organism long after the person survived the given infectious disease. This state is designated by the general term of *bacteria-carrying*.

Isolated into the external environment from the organism of the carrier pathogenic microbes may infect healthy people susceptible to the given infection.

The state of bacteria-carrying may develop after diphtheria, dysentery, typhoid fever and a number of other infectious diseases. An infectious patient may be a source of new infections in the very beginning of his illness and even at the end of the incubation period (typhus), for which reason one of the first and foremost meas-

ures of the anti-epidemic service is detection, isolation and rational treatment of infectious patients. It is necessary to diagnose the disease, hospitalize the patient and disinfect the focus as early as possible. Suffice it to say that if a typhus patient has appeared in a family, apartment or hostel, and was hospitalized within *the first 4-5 days* from the moment he has fallen ill, and if the necessary anti-epidemic measures have been carried out in the given focus of infection, no new typhus cases are usually observed among the people surrounding the patient. This example clearly shows the role played by early isolation of patients and by blocking the routes of transmission of infection.

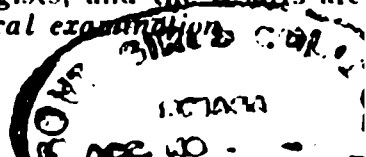
The responsibility of early diagnosis of an infectious disease rests with the physician of the polyclinic or ambulance services in cities, and with the district physician or physician's assistant in rural areas.

A physician or physician's assistant must strive to establish a *correct and early diagnosis* on the basis of the anamnesis, epidemiological data, careful examination of the patient and laboratory tests. It is at the same time necessary to hospitalize the patient, placing him as early as possible in a contagious hospital or contagious department of a hospital.

In addition to summoning a physician or physician's assistant to the patient's home, the patient's examination in a polyclinic and general epidemiological observations conducted by medical workers, considerable assistance in disclosing infectious patients is rendered by public sanitary inspectors; this is particularly important in rural communities.

The physician who has established a diagnosis of an infectious disease in a city notifies the district epidemiologist (by special messenger and telephone) and simultaneously summons an ambulance from the district disinfection centre to transport the patient to one of the contagious hospitals (in the larger cities this is done by order of the central distribution and evacuation office). Following the hospitalization of the patient a disinfection team from the disinfection centre disinfects the apartment or hostel in which the patient lived. Moreover, in cases of parasitic diseases (typhus) all persons living in the same apartment and those who had been in more or less close contact with the patient are given *sanitary treatment*, i.e., they bathe in a delousing centre, and their clothing, linen and bedding undergo chamber disinfection, according to the rules mentioned above.

The focus of infection, i.e., the apartment or hostel in which the patient was discovered, is subjected to an *epidemiological examination*, as a result of which it may be necessary to carry out additional anti-epidemic measures. In cities the epidemiological examination is conducted by district epidemiologists, and the results are recorded on a *special card of epidemiological examination*.



The aim of the epidemiological examination is to find the source of infection and the routes by which it was brought in and spread, and to work out the necessary anti-epidemic measures in accordance with the characteristics of the given infectious disease and the character of the focus (apartment, hostel).

While conducting an epidemiological examination, the physician or physician's assistant must not only collect all the necessary information from the patient himself and the persons surrounding the patient, but must also personally acquaint himself with the living conditions—diet, water supply and sewerage in the given apartment or hostel, and must decide on the measures necessary to prevent new cases of the disease. Thus, this examination is itself *an important anti-epidemic measure*.

Epidemiological and medical observation of the given focus is established in order that new cases of the same infectious disease may be discovered as early as possible and that the requisite sanitary and hygienic regimen may be adhered to. In such cases the physician (in rural areas the physician's assistant) examines at least three times a week all persons living in the same apartment (or other focus) where the patient sent to an infectious hospital was discovered. Special attention is devoted to the clinical signs which may help in the earliest possible diagnosis of new cases of the disease; for example, discovery of the Belsky-Filatov-Koplik sign (branlike scaling of the oral mucosa) will help in the early detection of measles. In the focus where a dysentery patient has been discovered, it is necessary to keep under constant observation people with an unstable stool and to subject them to thorough clinical examination, including inoculation of their faeces for dysentery bacteria.

In addition to the aforementioned measures, it is necessary daily to measure the temperature of all persons who were in contact with the patients in the focus of infectious disease over its longest incubation period (23 days in cases of typhus).

Children who have not had measles, varicella, whooping cough, scarlet fever or diphtheria and who are living in the same apartment or hostel in which a patient with one of these infectious diseases has been discovered are subject to *quarantine*, i.e., they are barred from nurseries, kindergartens, young pioneers' camps and schools until termination of the maximum incubation period. If repeated examinations by a physician or physician's assistant at the end of this period establish that the children are clinically absolutely healthy, the children are given a certificate admitting them to children's institutions.

Epidemiological examinations and observations of the focus of infection must aim at discovering bacteria carriers which play an important role in spreading many infectious diseases.

It is necessary to perform repeated laboratory tests of the faeces,

urine and bile, which make it possible to discover typhoid fever bacteria carriers.

District epidemiologists keep records of typhoid fever and dysentery bacteria carriers; these people must not be allowed to work in the water-supply system, food-processing enterprises, bakeries, dining rooms, lunch rooms, public kitchens, food-stores, kindergartens and nurseries, schools, hospitals, etc. Timely discovery of carriers is an important measure preventing bacteria carriers from becoming sources of new infections.

In rural communities all anti-epidemic measures are carried out by medical establishments. These medical establishments are responsible for discovering, recording, and hospitalizing infectious patients and for carrying out the necessary anti-epidemic measures. All cases of infectious diseases on the territory under the jurisdiction of a medical establishment must be immediately reported to the district department of public health. Upon outbreak of an epidemic the district epidemiologist is immediately summoned; the epidemiologist mobilizes all the anti-epidemic organizations of the district department of public health to stamp out the outbreak.

In cities, as well as in rural communities, notification about an acutely contagious patient must not be limited to sending information by special messenger to the district public health department. Each infectious case must be reported to the medical and sanitary establishment or the physician catering to the particular collective. If a child is diagnosed to have an infectious disease, it is particularly important immediately to notify the children's institution (nursery, kindergarten, young pioneers' camp) theretofore attended by the patient.

Upon appearance of cases of *especially dangerous infections* (plague, smallpox, cholera) the physician's assistant must immediately notify by telegraph or telephone, *observing the established rules*, not only the district and regional departments of public health, but also the Anti-Epidemic Administration of the USSR Ministry of Public Health. Special sanitation and anti-epidemic teams are immediately sent to the focus of particularly dangerous infection and a strict quarantine is established over a sufficiently large territory surrounding the given focus.

Obligatory hospitalization of infectious patients is an important factor of anti-epidemic work.

All patients suffering from acute infectious diseases and from exacerbation of chronic infectious diseases are usually subject to compulsory hospitalization, except certain categories of patients who may be isolated at home. It is particularly important to administer rational treatment to these patients.

Cholera, plague and smallpox patients, as well as persons who have been in contact with these patients, must be hospitalized under conditions of strict individual isolation.

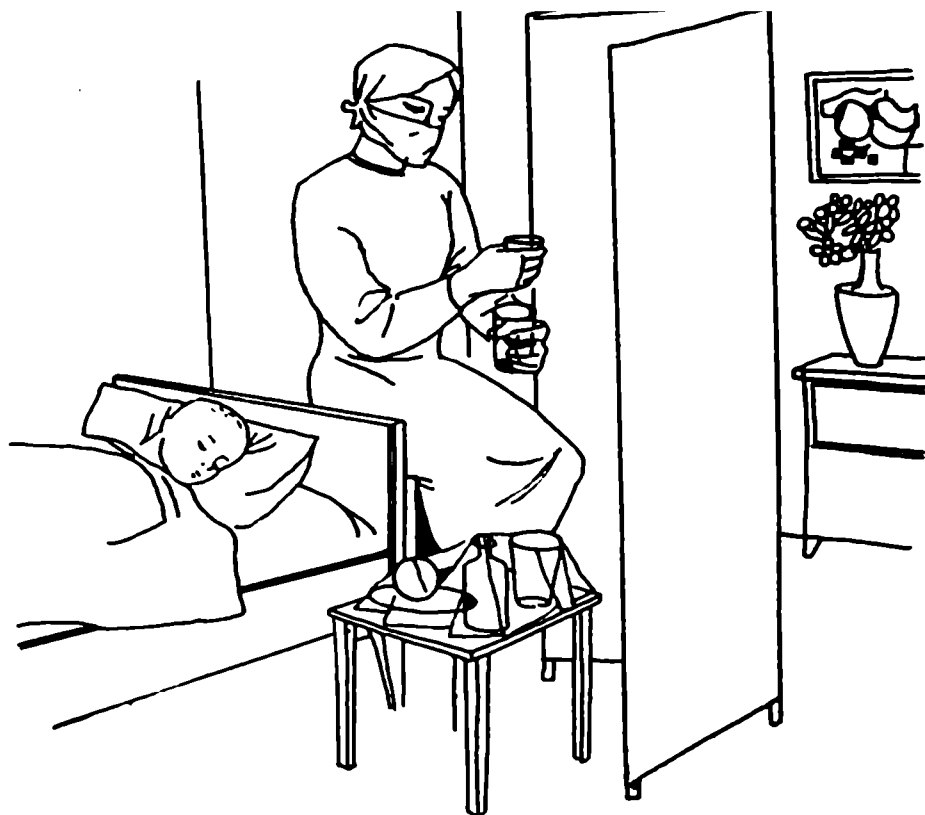


Fig. 14. Isolation of a patient at home

Certain infectious patients (influenza, uncomplicated measles) are either not hospitalized at all or are placed in contagious hospitals when the disease runs a severe course. But even when such patients are not hospitalized and are treated at home, they are under observation of a physician or physician's assistant and must be isolated (Fig. 14).

Patients are transported to contagious hospitals or divisions by *special ambulances* which are under the jurisdiction of the disinfection centre or the medical establishment.

Blocking the routes of transmission of infection includes hospitalization of patients with observance of all rules of isolation, sanitary and anti-epidemic measures in the focus of infection, establishment of a quarantine, elimination of violations of the rules of sanitation and hygiene (water supply, nutrition, sewerage), which are conducive to the spread of infection, and health education work.

All cases of zoonotic infectious diseases require more *intensive* sanitary and veterinary measures than usual.

Success of anti-epidemic measures in the focus of infection is achieved primarily through discovery of the concrete routes of transmission of the infection operating at the given moment. In most cases this makes it possible to adopt effective measures of blocking these routes.

It must not be overlooked, however, that some infectious diseases may have more than one route of transmission. For example, brucellosis may be contracted while caring for a sick animal (sheep, cow, goat), helping the animal in abortion or cleaning a cattle barn, i.e., when the causative agents of the disease (brucellosis bacteria) may invade the organism through cracks and abrasions in the skin. This route of transmission is characteristic mainly of workers of cattle farms, zootechnicians and veterinarians. However, brucellosis may also be contracted by persons who have no connections with agriculture whatsoever, but who either through ignorance or carelessness consume raw milk from animals affected with brucellosis.

These facts attest that concrete anti-epidemic measures must be carried out in accordance with the routes of transmission of infection, which sometimes may be combined.

It was already noted above that *preventive inoculations* are one of the methods of controlling infectious diseases.

As far back as several centuries ago Chinese physicians tried to create artificial insusceptibility to smallpox by introducing into the nose and rubbing into the skin of healthy people powdered crusts of smallpox pustules, which gave rise to mild forms of the disease.

From the middle of the 18th century *variolation*, i.e., inoculation of unmodified smallpox, was practised because the disease was extremely widespread all over the world. However, this method was prohibited because in a number of cases inoculation gave rise to actual smallpox.

E. Jenner (1749-1823), English scientist, searched over a period of 25 years for a rational method of inoculation against smallpox, one of the severest infectious human diseases. In 1796, Jenner brilliantly completed his research by using detritus, the content of the pustules on the skin of a calf to whom human smallpox was inoculated through incisures, for immunizing human beings to smallpox. Owing to the *passage* of the virus of smallpox through the organism of the calf the biological properties of the virus were greatly modified and its virulence was reduced with the result that it produced rather stable immunity to smallpox. Jenner's method was named *vaccination* and the inoculation material was named a *vaccine* (from the word *vacca* -cow).

Inoculations against smallpox began to be widely used at the end of the 18th century in different countries, including Russia; the smallpox incidence was thereby considerably decreased. However, the law did not make these inoculations compulsory.

Jenner introduced vaccination against smallpox purely em-

pirically, whereas the French scientist Louis Pasteur (1822-1895), who studied the processes of diminution of microbial virulence experimentally, established a *general principle* of producing vaccines from cultures of microbes subjected to certain extraneous influences which change the virulence of the cultures (limitation of oxygen supply, change in temperature at which microorganisms develop). In 1880-1886 he thus produced a vaccine against anthrax, which reliably protected animals against this disease. Later he produced a rabies vaccine to be inoculated to people bitten by rabid animals; this vaccine is still used as a highly effective agent for prevention of rabies.

Preventive medicine now widely uses a number of vaccines including not only killed, attenuated and living (the latter with *deeply modified* biological properties) cultures of bacteria, rickettsiae and filtrable viruses, but also *anatoxins* which are toxic products of bacteria treated with formalin to destroy their toxic properties and at the same time preserve their antigenic ability. Anatoxins are used for inoculations against diphtheria and tetanus.

All these biological preparations serve to create artificial immunity to corresponding infectious diseases by means of subcutaneous and cutaneous inoculations to healthy people. Methods for producing *chemical vaccines* have been elaborated in recent years; for example, a protective antigen is used for inoculations against anthrax.

In order to systematize the inoculations and to make a minimum of injections, *mixed vaccines* are used; a vaccine against whooping cough and diphtheria may serve as an example.

Cultures of typhoid fever bacteria killed by heating or by the action of formalin and used for inoculations against typhoid fever is an example of bacterial vaccines.

Smallpox and rabies vaccines may serve as examples of *living* filtrable virus vaccines; the filtrable viruses which are the causative agents of these diseases (smallpox and rabies) are modified under special conditions of cultivating the viruses.

As a rule, microbial vaccines are used for subcutaneous inoculations, for example, the vaccines for specific prevention of typhoid fever, paratyphoids A and B, cholera and brucellosis.

Some bacterial vaccines are used for *cutaneous vaccination*—rubbing into incisions on the skin made by a special “pen”. This is the way the living tularaemia vaccine is administered.

Virus vaccines may be administered both subcutaneously (rabies vaccines) and cutaneously (smallpox vaccines).

Inoculation of many types of vaccines produces rather stable immunity even when the vaccine is administered *only once*; vaccination against smallpox may serve as an example. Immunization to other infectious diseases required two or three administrations of a vaccine or anatoxin (inoculations against typhoid fever, cholera, diphtheria, tetanus, etc.). People bitten by rabid animals have to be inoculated with the rabies vaccine subcutaneously 20-40 times.

Not all inoculations for specific prevention of infectious diseases are equally effective. The most effective vaccinations are those against smallpox and rabies.

Quite satisfactory, but less marked immunity is produced by inoculations against anthrax and tularaemia. The existing methods of vaccination against typhoid fever and, especially, dysentery are still rather ineffective.

The duration of the immunity created by inoculation also varies within rather wide limits. For example, inoculations against smallpox are efficacious for 3-4 years, whereas inoculations against tularaemia ensure insusceptibility to this disease for a period of 3-5 years and are the most efficacious during the first two years.

It should be emphasized that not one of the existing methods of vaccination produces very long, especially lifelong, immunity, for which reason revaccination has to be resorted to; revaccination against smallpox and diphtheria is an example.

The rate of development of immunity as the result of inoculations varies; for example, it develops within 9-14 days in cases of vaccination against smallpox and only within 20-30 days in cases of inoculation against typhus.

Epidemiological indications sometimes necessitate unplanned and unscheduled vaccination and revaccination. For example, the entire population of a given area must be subjected to inoculations against smallpox upon appearance of the very first cases of this disease.

Living vaccines are the most effective, their immunizing effects approximating in certain measure to natural insusceptibility.

Considerable achievements in producing highly effective living vaccines have been made in the Soviet Union in recent years; for example, the tularaemia vaccine possesses potent immunizing action. Soviet scientists have produced new vaccines for inoculations against anthrax and brucellosis; they have also developed a dry smallpox vaccine.

It should be remembered that in immunized people the course of infectious diseases is characterized by a number of peculiarities. For example, in people inoculated against typhus the febrile period, if the disease develops, is usually shorter, intoxication is less pronounced and the eruption on the skin is not so abundant.

Inoculations against infectious diseases are made in special rooms of polyclinics, medical and sanitation centres of industrial enterprises and at other medical centres. The inoculations must be administered by well instructed nurses or physician's assistants under the general supervision of a physician.

The room for inoculations must be properly equipped; it must have the necessary furniture, a screen, a medicine chest, instruments, a sterilizer, and an adequate set of syringes and needles. Each inoculated person is registered in a special journal with indication of the date

of manufacture of the vaccine or anatoxin, the series of the preparation and number of the control test stated on the label of the ampule or vial.

Both vaccines and anatoxins should be stored in a dry dark place at a temperature of 4-5° C and used only during the period indicated on the label. Administration of a vaccine (especially in inoculations against typhoid fever) may sometimes be followed by undesirable side effects, namely, a rise in temperature, general indisposition, headache, nausea and vomiting. These reactions develop 10-12 hours after inoculation, but sometimes an inoculation may be immediately followed by temporary cardiovascular disturbances which require injections of ephedrine or camphor; these drugs must always be ready to hand during vaccinations. In some cases, for example, in active pulmonary tuberculosis, diseases of the liver and kidneys, inoculations are contraindicated. There are special instructions covering the exemption of certain people from compulsory inoculations.

Inoculations are administered first in so-called organized collectives (industrial enterprises, offices, schools). Inoculations against typhoid fever are usually administered from the end of February to the end of April.

The doses of vaccines for each inoculation are measured in numbers of microbial bodies.

Various vaccines and anatoxins may be combined for inoculations; for example, subcutaneous inoculations may be simultaneously administered against typhoid fever, paratyphoids A and B, dysentery, cholera and tetanus. Inoculations with a pertussis-diphtheria-tetanus vaccine have been elaborated. Each component of this vaccine serves as an antigen which produces specific immunity.

Inoculations against infectious diseases are in all cases an *auxiliary* means of preventing these diseases, whereas the main part is played by the general system of anti-epidemic measures which were described in detail above. The decisive importance of vaccination and re-vaccination for the prevention of smallpox may be recognized as an exception, but even this case requires the total complex of anti-epidemic measures.

Clinical Information

I.

INTESTINAL INFECTIONS

To classify various infectious diseases as intestinal infections, one must guide oneself by the clinical or epidemiological signs which determine their most important characteristics. The clinical picture of intestinal infections is characterized by a predominant affection of the gastrointestinal tract with general intoxication of the organism caused by the waste products of the causative agents (endo- and exotoxins) and perverted processes of metabolism, absorption and excretion of various products through the intestinal wall.

In many intestinal infections the causative agent does not penetrate beyond the intestinal wall and does not, as a rule, enter the general circulation (for example, in dysentery).

Some intestinal infections, however, are characterized not only by affection of the gastrointestinal tract, but also by *bacteraemia* as a result of which the causative agents penetrate into various organs and tissues where they produce a number of characteristic functional and anatomic changes (typhoid fever, paratyphoids A and B).

Epidemiologically the common feature of all intestinal infections is the mechanism of infection of man with the pathogenic microbes – through the mouth. The concrete routes of transmission of infectious intestinal diseases are also similar. As a rule, these diseases arise after a healthy susceptible person has consumed food or water contaminated with pathogenic microbes, or has introduced these microbes into the mouth with soiled hands.

A certain role in spreading these diseases is played by flies.

The causative agents of infectious intestinal diseases are excreted into the external environment mainly in faeces and sometimes, as, for example, in cholera, also in the vomitus. The causative agents of typhoid fever and of paratyphoids may be excreted not only in the faeces, but also in the urine.

TYPHOID FEVER (TYPHUS ABDOMINALIS)

Typhoid fever is a generalized acute infectious disease characterized by a cyclic course, definite temperature curve, general intoxication, bacteraemia and affection of the lymphatic apparatus of the small intestine through which

the infection implants itself in the organism upon entrance of the causative agent into the gastrointestinal tract.

Historical information. Although cases of typhoid fever were known in antiquity, the first correct clinical description of the disease was made by the French physician Bretonneau only in 1813, while the course of the disease was set forth in detail by P.C.A. Louis (also French) in his monograph in 1829. Typhoid fever and typhus, characterized by similar features during their early stages, were recognized as separate entities only in 1856.

An important contribution to the study of this disease was made by the outstanding Russian clinician S.P. Botkin who not only extended the knowledge of the course of the disease, but also gave a description of the fluctuating temperature curve which is most characteristic of typhoid fever.

In 1880 K. J. Eberth (Germany) and N. P. Sokolov (Russia) for the first time described the causative agent of typhoid fever they had discovered in the tissues and organs of persons who had died of this disease, but a pure culture of the typhoid bacillus was first produced by G.T.A. Gaffky only in 1884. The Widal serological test (1896) made laboratory diagnosis of typhoid fever possible while the method of isolating the typhoid bacillus from the patient's blood (haemoculture) was developed in 1902.

For a long time the treatment of typhoid fever patients was merely symptomatic. Such effective chemotherapeutic substances as synthomycin and levomycetin, which are synthetic antibiotics, have been produced and extensively used in medical practice only in recent years.

Aetiology. The causative agent of typhoid fever is the *Salmonella typhosa* (also called *Bacterium typhosum*) produced in pure culture by Gaffky in 1884. It is a motile gram-negative rod 3-3.5 μ long, with rounded ends. The motility of the microorganism is made possible by the numerous flagella covering its entire body. The most favourable medium for its growth both in the patient's organism and in artificial nutrients is bile; bacteria may be cultivated in agar, as well as in Endo's and Ploskiryov's media.

The bodies of typhoid fever bacteria contain O-antigen and the flagella- H-antigen.

The toxic influence exerted on the patient's organism by the causative agent is due primarily to the presence of poisonous substances (endotoxins) in the bodies of the typhoid fever bacteria, these substances being liberated from the bacterial cells on their death. In the external environment (water, milk, fruit, vegetables) typhoid fever bacteria may remain viable for a long time; for example, in cesspools they may endure for up to 30 days, in standing water—for 5 weeks, and in running water—about 8-10 days. In cold milk they remain alive for close to 35 days. Heating to 60° C kills them only in one hour, boiling—in 2-3 minutes. They are also killed by desiccation, direct sunlight and disinfectants (10 per cent chloride of lime solution, 2 per cent chloramine solution).

Epidemiology. The sources of infection are typhoid fever patients, convalescents or bacteria carriers. Bacteria are excreted into the external environment from the organism of patients, convalescents or carriers mainly in the faeces and partly in the urine with the result that water, foodstuffs and various other things may become contaminated.

Persons who have survived an attack of typhoid fever may become carriers and excrete the causative agent in the faeces or urine for a long time—a number of months or even years. From 5 to 6 per cent of typhoid fever patients become carriers of the infection. With the present-day low disease incidence in the USSR the most important part in typhoid fever epidemiology is played by bacteria carriers.

Typhoid fever bacteria enter the human body *only through the mouth* mainly with contaminated water or food, including milk.

The infection may be carried into the organism of a healthy person through the mouth with the hands contaminated by some objects with the excrements of a patient or carrier.

Cases of typhoid fever may be observed all year round; the seasonal increase in the disease incidence is due to the greater viability of the bacteria during the warm time of the year and the more frequent violations of the rules of hygiene and the normal dietary regimen. An important part in transmitting typhoid fever during the warm time of the year is also played by flies who carry on their legs and often in their intestines particles of excrements of typhoid fever patients or carriers containing the causative agent of the disease.

A very important part in the epidemiology of typhoid fever is played by faecal pollution of the sources of water supply (water lines, wells); the water-supply system must be kept under careful sanitary control. In epidemic outbreaks due to water pollution the incidence of typhoid fever increases rapidly over a period of 7-10 days; after elimination of the water routes of transmission of the infection the incidence drops, although an "epidemic tail" persists owing to transmission of the infection by flies and the contact with patients and carriers in the focus of infection.

Pathogenesis. After entering the gastrointestinal tract of a healthy susceptible person through the mouth typhoid fever bacteria, which possess motility and enzymatic activity, quickly implant themselves in the lymphatic apparatus of the intestines (Peyer's patches and solitary lymphatic nodules) and reach the adjacent regional (mesenteric) lymph nodes.

Following this the typhoid fever causative agent penetrates into the retroperitoneal lymph nodes. Hyperaemic and oedematous phenomena develop and small granulomas form in the mesenteric and retroperitoneal lymph nodes. The changes of the tissues in Peyer's patches and the solitary lymphatic nodules are characterized by strict cyclic recurrence and go through four stages, each lasting an average of about a week. These stages are as follows: (1) medullary tumefaction in which the lymphatic elements of the intestine become swollen, succulent, hyperplastic and considerably elevated above the surface of the intestinal mucosa; (2) necrosis of the tissues with gradual deepening of the ulcerous defect which may reach the outer (serous) coat of the intestinal wall; (3) disengagement of the necrotic and purulently altered tissues in the region of Peyer's patches and the solitary lymphatic nodules (Fig. 15) with growth of granulation tissue which covers the ulcerous defect; (4) stage of clean ulcers with formation of flat grey scars which do not produce stenosis of the intestine.

At the end of the incubation period the causative agent of typhoid fever gains entrance from the retroperitoneal lymph nodes into the thoracic duct and then into the general circulation with resultant bacteraemia which per-

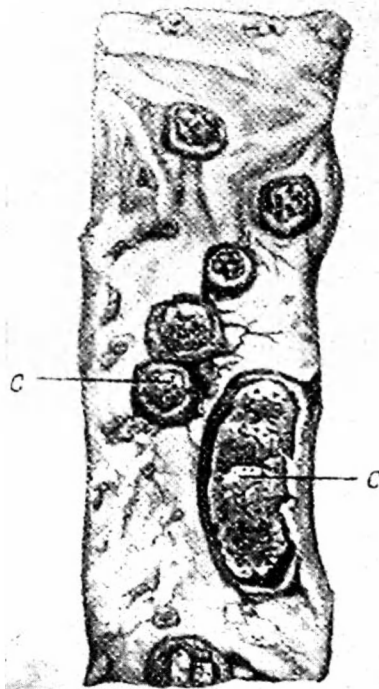
sists all through the febrile period of the disease; the latter circumstance is utilized for bacteriological diagnosis (blood inoculation for production of a haemoculture). The bringing of typhoid fever bacteria into various organs and tissues by the blood results in formation of tissue foci (granulomatosis) and makes it possible for the causative agent to re-enter the general circulation.

From the blood stream the typhoid fever bacteria penetrate into the bile ducts of the liver and into the gallbladder, where they find favourable conditions for multiplication, and then are again excreted into the intestine. The repeated invasion of Peyer's patches and the solitary lymphatic nodules, already sensitized by bacterial antigens, is followed by an allergic inflammatory reaction (similar to Arthus' phenomenon). This also results from penetration of Peyer's patches by typhoid fever bacteria directly from the blood stream.

The toxic effect produced by the causative agent on the patient's organism is due primarily to the presence of poisonous substances (endotoxins) in the bodies of the typhoid fever bacteria; these substances are liberated from the bacterial cells upon their death.

The result of intoxication of the organism is the "typhoid state"—depression of the central nervous system, changes in the cardiovascular apparatus (and especially in the protoplasmic dynamics) and metabolic disorders. The bacteremia maintains the febrile reaction and leads to formation of granulomas and diffuse degenerative-dystrophic processes in various organs, while the developing humoral and tissue immunity contributes to liquidation of the infectious process and complete recovery of the patients.

The enlargement of the liver and spleen is connected with deposition of rather large amounts of blood in them and is also due to proliferation of the cells of the reticuloendothelial system. The formation of roseolas is caused by the presence of the causative agent of the disease in the lymphatics of the skin.



Clinical picture. The incubation period averages 10-14 days, but may also be from 7 to 23 days.

Many typhoid fever patients exhibit a state of general intoxication sometimes accompanied by disturbances in consciousness; hence the name of the disease, which stems from the Greek word *typhos* meaning delusion.

The disease usually sets in *gradually*, with manifestations of general weakness, indisposition, jadedness, headache and considerable loss of

Fig. 15. Typhoid fever: formation of sequestrums (C) in the region of Peyer's patches and solitary follicles (from I. V. Davydovsky)

appetite; swallowing is sometimes accompanied by pain. This initial period of the disease (*the prodrome*) lasts from a few hours to two days and is followed by the febrile period.

One of the earliest symptoms of this period is a stepped, slow rise in temperature which only between the 5th and 7th days of the disease reaches a high level (usually 38.8-39.8°C) where it persists for two weeks and even longer. In 30-35 per cent of the cases typhoid fever sets in acutely.

Considerable general weakness, apathy, indifference to the surroundings, adynamia, loss of appetite and sleep disturbances are observed from the very first days of the disease; it is the considerable general weakness that soon impels the patient to take to bed. The patient usually complains of headache, insomnia, anorexia, constipation or, less frequently, diarrhoea. It should be noted that the complaints of the typhoid fever patients are limited to those enumerated above and are few.

The patient has a characteristic outward appearance: a languid, apathetic look and extreme pallor of the skin and the visible mucous membranes. Usually the patient displays no interest in his surroundings and seems to "have withdrawn into himself". In some cases loss of consciousness, hallucinations and delirium are possible. The intoxication of the organism increases with each passing day (Fig. 16).

The action of the endotoxins of typhoid fever bacteria extends to the entire nervous system, for which reason the clinical picture of the disease contains symptoms indicating pathology of the nervous system.

The respiratory organs are often affected (diffuse bronchitides and sometimes focal pneumoniae in the lower lobes of the lungs).



Fig. 16. Typhoid fever patient

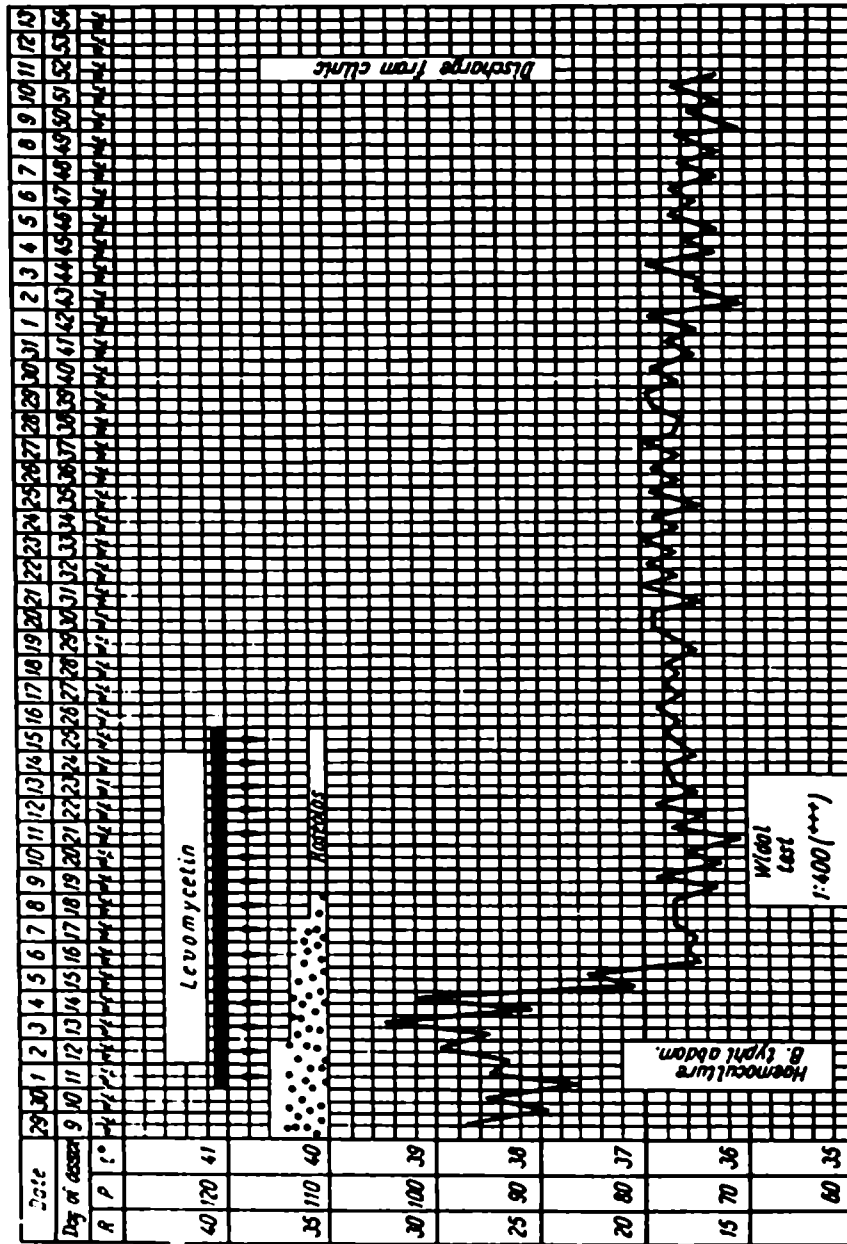


Fig. 17. Temperature curve of typhoid fever patient treated with levomycetin (the antibiotic was administered in accordance with the schema described on page 106)

18-year-old patient. Diagnosis: Typhoid fever (intestinal haemorrhage, relapse). fell ill October 1, 1950. Admitted to hospital October 14, 1950. Case history 13372. October-November 1950

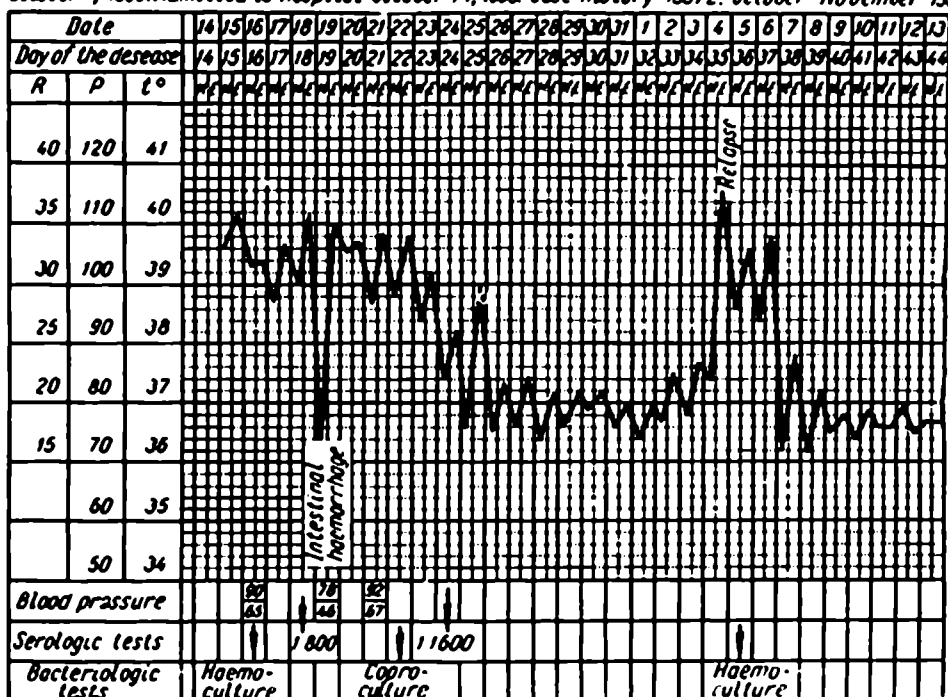


Fig. 18. Intestinal haemorrhage and relapse of typhoid fever in patient treated symptomatically

Persons who have survived typhoid fever acquire lasting immunity. During the first 2-3 days of the disease the blood shows moderate leucocytosis which is later replaced by leucopenia characteristic of typhoid fever (up to 4,000-3,000 leucocytes per 1 cu mm of blood) with aneosinophilia, neutropenia and a shift of the formula to the left, as well as relative lymphocytosis (35-60 per cent lymphocytes). Sometimes the disease is accompanied by leucocytosis.

The clinical picture of typhoid fever may often fail to show the above-described characteristic features. Acute, moderately severe and severe forms of uncomplicated typhoid fever are distinguished. The differences between these forms are based on the extent of intoxication and intensity of the pathological symptoms, mainly on the part of the cardiovascular and nervous systems.

Sometimes, soon after the development of the clinical picture of typhoid fever has started, the further course of the disease is interrupted and the patient quite rapidly recovers (*abortive form* of typhoid fever). A haemoculture of the causative agent of the disease may play a decisive role in the diagnosis of this form.

In a number of cases the clinical symptomatology is very scant;

in such *atypical*—mild and mildest—forms (*typhus abdominalis levis*, *typhus abdominalis levissimus*) intoxication is very slight, the typhoid state is absent, the temperature does not rise above 38°C, the spleen and liver are not or are but slightly enlarged, and there is no eruption on the skin. Such cases are very difficult to diagnose and may be identified mainly by laboratory methods (primarily by production of a blood and bile culture).

Ambulatory typhoid fever is a special atypical form of the disease; patients affected with this form of the disease feel so satisfactory that they are able to visit the physician at the dispensary; there have been cases, however, when such patients died as the result of complication with perforative peritonitis, although they were not known to have typhoid fever while alive and they had not observed the necessary bed and dietary regimen. To diagnose ambulatory typhoid fever, it is necessary to make wider use of blood, bile, urine and stool cultures.

In persons who have taken a full course of *inoculations* against typhoid fever (by means of trivaccine, pentavaccine or polyvaccine) the disease runs for the most part an atypical course with an *acute* or *subacute* onset, short febrile period (8-15 days), slight intoxication and very scant eruption on the skin; the blood, despite leucopenia and relative lymphocytosis, which are characteristic of typical cases of the disease, often contains eosinophils (1-2 per cent); complications are very rare.

A careful analysis of all the clinical data and repeated blood, bile, urine and stool cultures for the purpose of isolating typhoid fever bacteria help to diagnose these atypical forms.

In *children* 7-8 years of age typhoid fever has a number of peculiarities; the onset of the disease is usually acute, with marked intoxication, rapid elevation of the temperature to a high level by the 3rd-4th days of the disease, and subsequent brief remissions. Relative bradycardia and a dicrotic pulse are often absent. Vomiting and diarrhoea are not infrequently observed. The haemogram is not characteristic; leucocytosis and retention of eosinophils in the blood are possible.

Diagnosis. Typhoid fever is diagnosed on the basis of the clinical picture of the disease with due consideration of epidemiological data (possibility of infection from typhoid fever patients or carriers, disease incidence in the given locality, season) and the results of laboratory tests which must, as far as possible, be used to confirm the clinical diagnosis.

The most valuable diagnostic method of laboratory test is inoculation of 10-15 ml of the blood taken from the patient's vein in 100 ml of sterile bile broth or Rappoport's medium. This inoculation is made directly at the patient's bedside under strictly aseptic conditions (passing the neck of the vial and its cotton plug over the flame of an alcohol burner, etc.). Immediately after the blood inoculation

the vial is placed in a thermostat, at 37°C, where the bacteria are grown for 24 hours. The laboratory gives the preliminary answer in 48 hours and the final answer on the fourth day after the inoculation. To obtain a blood culture of the causative agent in atypical cases, the blood may be inoculated on the very first day of the disease.

The probability of isolating bacteria from the blood is the greatest precisely in the first days of the disease. However, a blood culture may also be obtained at later periods of the disease. If the inoculation is made after the tenth day of the disease, at least 15 ml of blood must be taken from the vein, and a few minutes before the blood is taken 0.6 ml of 1:1,000 adrenalin solution must be injected subcutaneously. Inoculations must be widely utilized to produce blood cultures.

The diagnosis of typhoid fever may also be confirmed by a positive Widal reaction. For this test 2-3 ml of the patient's blood is sent in a test-tube to a bacteriological laboratory. The Widal reaction is considered positive in a 1:200 titre and in greater dilutions with increasing titres in repeated tests. This test may be performed from the 8th or 9th day of the disease. If the Widal test cannot be performed locally, a sheet of cellophane with two or three separate dried drops of the patient's blood serum should be sent to the nearest laboratory. In the laboratory each piece of cellophane with a drop of the patient's blood serum is cut out, soaked in physiologic solution, and the Widal test is performed with the resultant extract containing the antibodies.

The Widal agglutination test must be performed in all cases with O- and H-antigens of typhoid fever bacteria in the form of a killed culture; determination of the titres of only O-agglutination is of diagnostic importance.

Owing to the resemblance of the clinical picture of typhoid fever to that of a number of other infectious diseases a careful differential diagnosis is necessary.

To distinguish typhoid fever from *typhus* in the first 4-6 days of the disease, it should be remembered that typhus patients are characterized by general neuropsychic excitement, hyperaemia and puffiness of the face, congestion of the sclerae and conjunctiva of the lids, earlier enlargement of the spleen, tachycardia, and usually moderate leucocytosis (10,000-13,000 leucocytes per 1 cu mm of the blood) always with neutrophilia and a nuclear shift to the left. A rather plentiful roseolous or roseolous-petechial eruption appears on the 4th-6th days in cases of typhus (Fig. 19 and Table 3).

In identifying typhoid fever it is necessary to differentiate it from *miliary tuberculosis*. The following symptoms of *miliary tuberculosis* must be taken into consideration: considerable fluctuations of temperature, tachycardia, dyspnoea, cyanosis and numerous lesions the size of a millet seed (shadows of perifocal inflammation of pulmonary tissue) revealed by roentgenograms of the lungs.

Brucellosis which in the early period of the disease sometimes resembles typhoid fever is particularly characterized by chills, frequent and profuse perspiration, pains in the muscles of the neck and in the lumbosacral region, and later by pains and objective changes in the joints (swelling, limited mobility) and formation of fibrositides (see Fig. 19).

During the first 2-3 days of the disease it is sometimes necessary to differentiate typhoid fever from *influenza*. The latter disease is characterized by a rather acute elevation of temperature, a brief febrile period, pains in the region of the supraorbital ridges and eyeballs, and tracheitis; rhinitis and coughing are sometimes observed.

In establishing a differential diagnosis it is necessary to remember the possibility of *malaria*, especially in areas where it is widespread and mainly in fresh cases with continuous fever during the first 6-8 days of the disease; later, malaria patients exhibit characteristic attacks of fever—chills, pyrexia with a subsequent drop in temperature and profuse perspiration. In such cases the final diagnosis is based on the presence or absence of malarial plasmodia in a thick drop of the patient's blood upon its repeated examination.

Laboratory tests help to differentiate typhoid fever from the aforementioned diseases.

Complications. The course of typhoid fever may be disturbed by various complications arising in addition to the main pathologic process. Development of focal pneumonia was a rather frequent complication before the introduction of antibiotics into therapeutic practice. Pneumonia may develop in the very first days of the disease and is revealed by clinical (dull tympanic sound and crepitant rales in the inferoposterior parts of the lungs, sometimes coughing and a slight discharge of sputum) and roentgenological data. In some cases pneumonia may develop during later periods of the disease.

Thrombophlebitides (most commonly affecting the large veins of the lower extremities), parotitides (inflammation of the parotid gland) and otitides (inflammation of the middle ear) may develop between the 18th and 22nd days of the disease.

Various complications on the part of the nervous system usually in the form of pareses and paralyses predominantly affecting the ulnar nerve and the brachial plexus are observed, although comparatively rarely. A picture of meningo-encephalitis sometimes develops in severe cases of typhoid fever.

Some patients may, during late periods of the disease (between the 16th and 25th days), develop collapse, i. e., acute vascular insufficiency as a result of a rapid redistribution of the blood from the peripheral vessels to the vessels of the abdominal organs; the symptoms of collapse are sudden extreme pallor of the skin, perspiration, thready pulse, drop in blood pressure and an uneven drop in temperature. Myocarditis sometimes developing during late periods of the

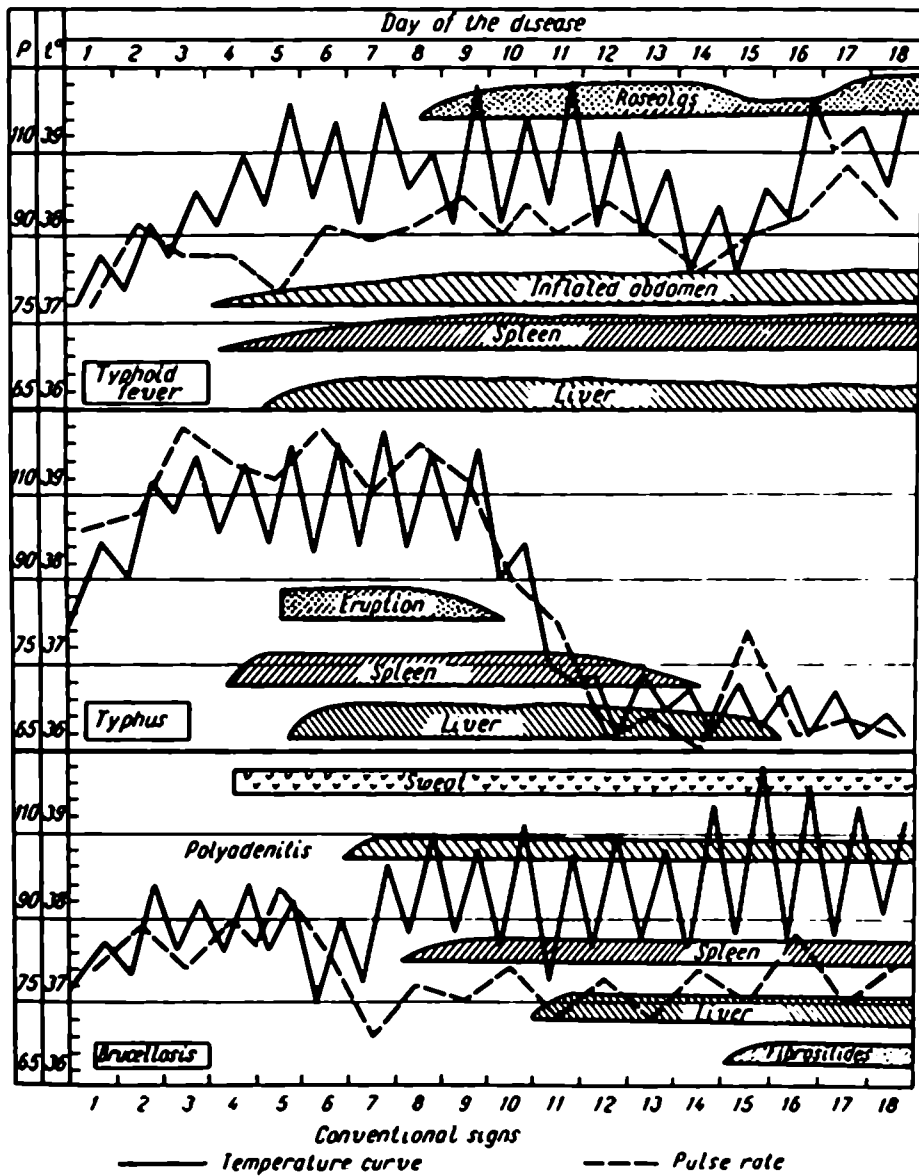


Fig. 19. Most important differential-diagnosis signs of typhoid fever, typhus and brucellosis

disease must be mentioned as one of the important complications of typhoid fever; the symptoms of this complication are tachycardia, extension of the percussion borders of the heart, dull heart sounds and systolic murmur; the electrocardiogram shows a flattened or negative *T* wave and depression of the *S-T* segment, especially in the chest leads.

The intestinal complications include intestinal haemorrhages which arise on destruction of blood vessels in the region of necrosis of a Peyer's patch or a solitary lymphatic nodule. The development of haemorrhages is fostered by a diminished ability of the blood to clot, a decrease in thrombocytes and insufficient formation of prothrombin in the liver. Intestinal haemorrhage manifests itself in sudden pallor of the patient, a sharp acceleration of the pulse, and a drop in blood pressure and temperature (see Fig. 18) to normal or subnormal figures. Several hours later the patient's faeces show an admixture of fresh or altered (black) blood, depending on the time of the bowel movement. If the patient has a stool several hours after the haemorrhage, the stool is dark, tarry (melaena). Intestinal haemorrhages may recur in the course of one day or several days in succession. They may be massive (up to 500 ml of blood) or very slight, thereby determining the clinical symptoms and consequences of the haemorrhages.

Intestinal haemorrhages most commonly appear in complicated cases of typhoid fever between the 16th and 25th days of the disease. Perforation of an intestinal ulcer is particularly dangerous; if no aid is administered in due time, this complication leads to development of peritonitis. In some cases of perforation patients experience a sudden sharp pain in the abdomen, the skin rapidly pales, the face becomes drawn, drops of sweat appear on the forehead, the pulse is sharply accelerated and is of low tension and weak filling (phenomena of collapse). Now and then retching is observed. The abdominal muscles, especially in the suprapubic and iliac regions are tense. The tongue becomes dry, and signs of peritoneal irritation appear, tension of the anterior abdominal wall usually being a positive Shchotkin-Blumberg's sign; intestinal peristalsis either fails to be auscultated through a phonendoscope or is weakened; percussion shows the liver to be displaced upward because of the air present in the abdominal cavity; the number of leucocytes in the blood increases in the very first 2-3 hours following perforation; leucopenia present before the perforation of the intestine is replaced by leucocytosis. Upon the least suspicion of perforation of intestinal ulcer a surgeon must be consulted and the patient must be transferred to the surgical division of the hospital; confirmation of this diagnosis must be immediately followed by surgical intervention.

The late days of the disease, for example, the 3rd or 4th weeks in cases untreated with antibiotics, are the most dangerous period of typhoid fever because of the possible development of serious compli-

cations. The possibility of relapses observed in cases of symptomatic treatment, as well as in those treated with antibiotics, has already been mentioned.

Patients treated with antibiotics have but few complications and no purulent complications at all. But even in cases treated with antibiotics collapses, intestinal haemorrhages and perforations of intestinal ulcers are sometimes observed, for which reasons patients must be kept on a diet and in bed.

Treatment and care of patients. Complete rest, cleanliness of the hospital ward, plenty of fresh air, and a temperature of 19-20°C are indispensable conditions for typhoid fever patients.

In the regions of the sacrum, scapulae and buttocks, where the pressure produced by the weight of the body is the greatest, the patient's skin, especially in severe cases, must be rubbed down with camphor alcohol or vegetable oil. It is good to sponge the body with warm water containing cologne or mint tincture since it reflexly improves circulation and respiration. In severe cases the oral cavity must be wiped with a cotton tampon soaked in a 2 per cent boric acid solution. All other patients must rinse their mouths with the same solution twice a day and, if possible, brush their teeth.

In cases of intense headaches it is necessary to apply an icebag to the patient's head for 15 minutes with intervals of the same duration. To prevent pneumoniae which are fostered by hypostases, the patients should be turned in bed as often as possible.

Patients must be fed 4-5 times a day; debilitated patients must be patiently fed by the hospital personnel.

The food given to patients must be easily assimilable, highly caloric (up to 3,000 Cal per day), vitamin-rich, finely-ground and semiliquid. Under no circumstances may the patients be given irritating, seasoned or coarse food.

During the febrile period and for the first 8-10 days following the drop in temperature the diet of typhoid fever patients must contain no foods capable of mechanically or chemically irritating the gastrointestinal tract. The food must be as varied as possible. The patient's diet must include white zwieback (75 g per day), white half-stale bread (150-200 g), salmon or sturgeon caviare (25 g), fresh butter (25-40 g), chicken-egg yolks (2), fresh curds (200 g), sour cream (75 g), sour milk, kefir or acidophilous soured milk (up to 500 g of one of these dairy products).

Hot dishes are served in the form of broths (250 g) made of lean beef or chicken; soup with semolina and quenelles, and rice or oatmeal soups are very healthful. As second courses the patients may be given for dinner steamed meat or fish balls with mashed potatoes to which 10 g of fresh butter is added, well-boiled vegetables which do not contain large amounts of cellulose, well-cooked semiliquid cereals (buckwheat or rice; the latter is cooked in milk diluted with water), 10 g of fresh butter being added to each portion, or fresh boiled

fish with vermicelli. The patients should be given fruit and berry jellies, stewed, well-sieved fruit, sweet varieties of fresh fruit, peeled and pitted, ground fresh apples, baked apples, fruit preserves, mousses, creams, natural fruit and berry juices which contain a lot of vitamins (especially black currant and orange juices). The patients must be given plenty to drink, particularly rose hips syrup, alkaline mineral waters, sweet tea and small amounts of coffee.

In recent years medicine has acquired new highly effective medicinal preparations for the treatment of typhoid fever, namely, synthomycin (chloramphenicol) and levomycetin.

Levomycetin is administered per os in a dose of 0.5 g 6 times per day until the temperature drops, which occurs on an average 3-6 days after the beginning of the treatment; the preparation is given in the same doses for another 2-3 days after the drop in temperature. Then it is administered in a dose of 0.5 g 4 times per day for 7-8 days until the tenth day of normal temperature inclusive (see Fig. 17). A complete course of treatment takes from 32 to 40-42 g of levomycetin. This scheme of treatment is the most rational.

In patients treated with antibiotics the intoxication quite soon diminishes, the temperature is normalized, the various other morbid symptoms mitigate and then totally disappear.

As practice has shown, treatment of typhoid fever patients with levomycetin is the most effective when administered as follows: 0.5 g 6 times per day up to the 2nd day of normal temperature (inclusive) and 0.5 g 4 times per day from the 3rd to the 10th day of normal temperature.

During the treatment with synthomycin or levomycetin various side effects (toxic and allergic)—nausea, vomiting, diarrhoea, abdominal pains, and drug eruptions—may sometimes be observed. In most cases they do not contraindicate further use of the preparation, although for individual patients the treatment with antibiotics has to be cancelled because of marked intolerance phenomena.

Despite the general success of treatment with antibiotics individual patients may suffer relapses or become carriers. In view of the possibility of late relapses patients treated with antibiotics are not discharged from the hospital before 23 days following the normalization of temperature. Bacteria-carrying is usually developed by persons who have survived pathologic disturbances in the biliary-hepatic system—cholecystitides, cholangitides and hepatitides (mainly by women). Urinary bacteria-carrying due to the presence of typhoid fever bacteria in the urinary tract is observed much less frequently.

During the treatment it is necessary to support the patient's cardiovascular functions; it should be noted that the functions of the vessels are mostly affected, for which reason, when indicated, the patient is administered per os or in injections ephedrine (0.6 ml of a 5 per cent solution) and cordiamine (nikethamide) (20 drops per os or

2 ml subcutaneously), the administration of these preparations being repeated 3-4 times per day, according to indications.

In cases of persistent insomnia the patients are given hypnotics (luminal, barbamyd [amytal sodium] and medinal [barbital sodium]).

It is particularly important to identify the various complications and take measures to eliminate them.

In cases of intestinal haemorrhage the patient is temporarily given no food (for 10-12 hours), but may be given something to drink in small portions. To terminate the intestinal haemorrhage, the patient should be given a transfusion of 125-150 ml of blood of the same group or group 1(0), since it acts haemostatically. Following the haemorrhage the patient is administered per os a 10 per cent calcium chloride solution (in table-spoonfuls) and vitamin K (vicasol, in single doses of 0.015 g); these preparations are given 3 times per day for 2-3 days.

Perforation of an intestinal ulcer, if the diagnosis is established with adequate precision, serves as an indication for an immediate operation. In cases of collapse the patient is administered ephedrine, injections of a 5 per cent glucose solution, and of physiologic solution by the drip method.

In typhoid fever the prognosis is determined by the severity of the disease, the character of complications and the therapeutic measures.

Disinfection and rules for discharging patients. The patient's excrements in the bedpan or chamberpot are covered for 3 hours with a similar amount of a 10 per cent chloride of lime solution or are mixed with dry chloride of lime and allowed to stand for the same period of time, following which the detoxicated excrements may be poured out into a toilet or cesspool.

After feeding or examining the patient or performing any other manipulation the attending personnel must thoroughly wash their hands with a 0.5 per cent chloramine solution and then with hot water and soap. After meals the patient's dishes must be sterilized by boiling. The patient's linen is soaked for 1 hour in a 0.5-1 per cent chloramine solution and then boiled in lye tanks. Convalescents are not allowed to sit up in bed until 8-10 days after normalization of the temperature and to get out of bed until still later, i. e., only after adequate restoration of the cardiovascular functions impaired by the disease. Cured patients are discharged from the hospital after disappearance of the clinical manifestations of the disease, but not before the 14th day of normal temperature in cases where they were not treated with antibiotics (synthomycin or levomycetin) and on the 23rd day of normal temperature in cases treated with antibiotics.

To control bacteria-carrying, it is necessary to examine the patient's faeces and urine for typhoid bacteria three times (on the 12th, 15th and 18th days of normal temperature) and to inoculate the pa-

tient's bile in Rappoport's medium or agar on the 14th or 16th day of normal temperature. If the bacteriological tests cannot be performed, it is necessary to adhere to the aforementioned periods of isolation of convalescents. If the person who recovered from typhoid fever was a carrier at the time of his discharge from the hospital, cultures of his stool, urine and duodenal contents must be made five times within the first month. The epidemiologist takes the carrier under general observation and gives him and the people surrounding him instructions in hygiene.

If the person who has recovered from typhoid fever is a worker of the food industry, water-supply system or children's institutions, he is not allowed to work for one month during which the aforementioned bacteriological tests are performed. If all the tests prove negative at the end of the month following the person's discharge from the hospital, the given person may be allowed to return to work, but must be examined for typhoid fever bacteria-carrying every 3 months for a period of 5 years.

Prevention. General sanitary and hygienic measures—proper water supply and sewerage in populated areas, extermination of flies, observance of rules of personal hygiene, especially washing the hands before meals—play a very important part in preventing typhoid fever. It is very important to reveal bacteria carriers and to dismiss them from work in the food industry, grocery and provision shops, lunch rooms, dining-rooms, hospitals and children's establishments. All typhoid fever patients are subject to compulsory hospitalization, while the focus of the disease must be disinfected.

Inoculations with a typhoid vaccine help to reduce typhoid fever incidence. If the person immunized against typhoid fever contracts the disease just the same, the disease runs a rather favourable course. The population must be regularly given instructions in hygiene.

If the population is supplied with water from wells, the framework of the wells must be properly made and the wells must have clay or concrete keystones to prevent water from flowing from the surface of the earth back into the wells.

PARATYPHOID FEVER A AND PARATYPHOID FEVER B (PARATYPHUS ABDOMINALIS A AND PARATYPHUS ABDOMINALIS B)

Paratyphoid fevers A and B are closely related to typhoid fever in their clinical pictures, are absolutely identical to the latter in their epidemiological characteristics, but differ from it as to the properties of the causative agents.

The difference between the causative agents of paratyphoid fever A (*Salmonella paratyphosa*), paratyphoid fever B (*Salmonella schott-*

mülleri) and typhoid fever (*Salmonella typhosa*) consists only in the peculiarities of some of their biological properties—the antigenic pattern of the bacterial cell, enzymatic, biochemical activity and the ability of the bacteria to agglutinate by specific serums.

Man contracts paratyphoid fever A and paratyphoid fever B when virulent causative agents of these diseases gain entrance into his mouth.

The incubation period of paratyphoid fevers A and B is on the average 2-3 days shorter than that of typhoid fever. In all three diseases often commonly referred to as *typhoid-paratyphoid fevers* it is the lymphatic apparatus of the small intestine, i. e., Peyer's patches and solitary lymphatic nodules that are affected, and ulcers are formed.

In paratyphoid fevers the intoxication of the organism is not so intense as it is in typhoid fever, but bacteraemia persists all through the febrile period. An attack of these diseases confers lasting immunity.

The clinical pictures of paratyphoid fevers A and B are practically identical with that of typhoid fever and differ from the latter only in some details. However, certain characteristics of these diseases should be remembered; for example, repeated chills with temperature variations are possible in paratyphoid fever A, and relapses are observed more frequently than in typhoid fever. Paratyphoid fever B is sometimes characterized by an acute onset, rather plentiful roseolous eruption and at times herpetic eruptions on the skin of the upper lip near the nostrils.

Diaphoresis and moderate leucocytosis with eosinopenia are not infrequently observed in paratyphoid fevers A and B.

The clinical course of paratyphoid fever B sometimes resembles that of food poisoning of salmonellae etiology (abdominal pains, diarrhoea, nausea or vomiting); at the same time the patients exhibit an enlarged spleen and leucopenia with relative lymphocytosis. The question of diagnosis is decided by bacteriological stool and vomitus tests, and blood cultures; in addition to these tests it is necessary to perform the agglutination test with a water suspension of salmonellae and a homologous strain.

As a rule, paratyphoid fevers A and B run a more favourable course than typhoid fever and less frequently produce such severe complications as perforation of intestinal ulcer and intestinal haemorrhages. However, all these differences are quite conditional and far from constant. Paratyphoid fevers A and B may be reliably distinguished from typhoid fever only by laboratory diagnostic methods (cultures of the patient's blood, urine, stool and bile, and the Widal test with appropriate antigens).

If these tests cannot, for some reason, be performed, especially when the clinical picture attests typhoid-paratyphoid fever, it is necessary to diagnose the condition as typhoid fever and hospitalize the patient with this diagnosis.

The methods of diagnosis and treatment, the conditions for hospitalizing patients and the time for discharging them, as well as carrying out anti-epidemic measures in cases of paratyphoid fevers A and B, are the same as in typhoid fever. It must also be emphasized that paratyphoid fevers occur much less frequently than typhoid fever; paratyphoid fever A is observed particularly rarely.

People who have survived an attack of paratyphoid fevers A and B may become acute (for about 3 months) or chronic carriers. As in cases of typhoid fever bacteria-carrying, the carriers of paratyphoid infection are not allowed to work in the food industry, provision shops, dining-rooms, lunch rooms, restaurants, water-supply structures, etc.

To reveal carriers repeated urine and bile cultures in Rappoport's medium with reinoculation in agar, and stool cultures in Kauffmann's and Endo's media are required.

FOOD POISONING

Food poisoning represents an extensive group of acute human infectious diseases caused by various microbes and their toxins on consumption of infected foodstuffs. The diseases are accompanied by general intoxication, elevated temperature, cardiovascular disorders (to the point of collapse) and gastrointestinal symptoms.

Aetiology. The causative agents of food poisoning constitute a large group of bacteria (close to 530 different representatives), the most important of which are the salmonellae named in honour of microbiologist Daniel Elmer Salmon; this group includes the most commonly occurring bacteria (*Salmonella typhimurium*), Gärtners bacilli and many others. In addition to salmonellae food poisoning may be caused by conditionally pathogenic bacteria, for example, the *Proteus vulgaris*, staphylococci, streptococci, and even the colon bacillus. The development of food poisoning caused by conditionally pathogenic microbes is determined by massive invasion, diminished defense properties of the organism, and disorders of the gastric and intestinal functions.

The causative agents of food poisoning may live in infected foodstuffs for a number of days.

Epidemiology. Consumption of meat and fish infected with salmonellae is the most common cause of food poisoning.

The meat of cattle may become infected during their lifetime because naturally occurring diseases caused by salmonellae are sometimes observed in cattle and pigs; moreover, the slaughter, dressing and transportation of the carcasses under unsanitary conditions may also foster infection of the meat. Analogously, failure to observe the rules of food hygiene in salting fish often resulted in its infection (mainly with Gärtners bacteria), as well as infection of the foods prepared from fish.

It should be emphasized that in cases of inappropriate storage and processing of meat and fish products in kitchens there is a serious danger of infecting these products with the result that single cases, as well as outbreaks of food poisoning, have repeatedly been observed among the people who consumed them.

In addition to meat and fish, food poisoning may be caused by other foods infected in the process of their preparation or storage. There have been cases of human infection caused by consumption of duck and goose flesh, as well as duck and goose eggs. Sporadic cases and outbreaks of food poisoning caused by consumption of infected milk have been repeatedly observed.

Food poisoning may be caused by pathogenic staphylococci if the food, especially cream for cakes and pastries, which is a good nutrient medium, was prepared by persons affected with pyodermas of the hands.

Failure to observe rules of sanitation and hygiene in places where food is prepared or distributed may lead to infection of foods with pathogenic and conditionally pathogenic (*Proteus*, colon bacillus) microbes. Favourable conditions for multiplication of microbes and accumulation in the foods of toxic substances formed when the microbes die are created by the grinding of foodstuffs (patés, meat-jellies, force-meats, boiled sausage) and in cases of their unsanitary storage, as well as without their requisite cooling. The warm seasons are conducive to multiplication of pathogenic microbes in foodstuffs with the result that cases of food poisoning are more common during these seasons; however, failure to observe the rules of storing foodstuffs under refrigeration at any time of the year leads to multiplication of the causative agents of food poisoning in them.

Food poisoning occurs mainly as single (sporadic) cases, although mass outbreaks are also possible, if several people have consumed the same food. Outbreaks of food poisoning are characterized by a short incubation period and mass incidence among people who have consumed the same food, as well as an approximately simultaneous onset of the disease. Owing to Soviet sanitary laws which provide for continuous control of food industries and trading establishments, dining-rooms, lunch-rooms, restaurants, etc., the number of cases and, especially, outbreaks of salmonellae food poisoning in the USSR are decreasing with each passing year.

Pathogenesis and pathologic anatomy. The development of the pathologic process in food poisoning is fostered by intoxication of the organism and the direct influence of the causative agents of the disease on the mucous membrane of the gastrointestinal tract. Some forms of food poisoning are accompanied by bacteraemia with the causative agent multiplying in the tissues; this occurs in diseases caused by Breslau's bacilli (*Salmonella typhimurium*). Disturbances in the cardiovascular and nervous systems associated with the presence of specific intoxication, as well as symptoms of acute gastroenteritis,

determine the clinical picture of food poisoning. Autopsies of persons who died of food poisoning reveal oedema and hyperaemia of the mucosa of the small intestine and numerous haemorrhages in the intestinal wall. The spleen and liver are enlarged and their parenchymatous cells are degenerated.

Clinical picture. The incubation period is most commonly 8-14 hours, but it may vary from 2 to 24 hours and sometimes longer.

Classification. On the basis of the latest scientific conceptions the following conditions must be distinguished according to their clinical course: (1) acute salmonellal gastroenteritis, (2) acutest salmonellal gastroenteritis, (3) typhoid form of infection (salmonellosis typhoides), (4) salmonellal enterocolitis (enterocolitis salmonellosa), (5) salmonellal gastroenterocolitis, and (6) salmonellal sepsis. A clinical variant of salmonellal gastroenteritis is gastroenterocolitis which may be considered a separate disease entity. In individual cases the clinical aspect of the disease may be limited to the picture of isolated acute gastritis.

The course of the disease described below corresponds to the typical acute form of salmonellal gastroenteritis.

As a rule, food poisoning begins acutely with general indisposition, nausea, repeated vomiting and abdominal pains; these symptoms are followed by a frequent liquid stool of a faecal character (acute gastroenteritis). The intoxication manifests itself in pallor of the skin, a pulse of low tension and diminished filling, arterial and venous hypotension (usually the blood pressure is lowered), dull heart sounds, tachycardia, and intense thirst; the tongue is dry and coated, the abdomen is inflated and painful in the epigastric region. The temperature often reaches a high level but the duration of the febrile period is short (2-5 days). In some cases (gastroenterocolitic form of the disease) the excrements contain a slight admixture of mucus and even blood in the form of streaks, which creates a certain resemblance of dysentery. The blood picture is characterized by leucocytosis and neutrophilia.

In cases of considerable intoxication the disease runs a severe course. In these cases the blood is thickened, which is attested by high haemoglobin and erythrocyte figures, the organism becomes dehydrated, and acute vascular insufficiency (collapse) and convulsions are possible.

In cases where the disease runs a favourable course and with early rational treatment all morbid phenomena abate within 4-6 days. Sometimes prolonged excretion of bacteria is possible.

The above description is one of a typical course of food poisoning, but in addition to these typical forms of diseases there may also be cases of food poisoning with different clinical pictures (see classification).

A special clinical form of food poisoning is *acutest* salmonellal gastroenteritis (gastroenteritis acutissima salmonellosa). The disease develops extremely rapidly; the patients suffer from repeated ex-

haustive vomiting, have a frequent liquid stool (water faecal masses with a fetid odour) and exhibit sharp dehydration of the organism, pallor of the skin with cyanotic lips, a thready pulse, arterial hypotension, low body temperature and convulsions. This grave condition may constitute a serious threat to life, especially in cases where therapy was begun late.

The *gastroenterocolitic* form of food poisoning may very greatly resemble acute dysentery (see chapter on differential diagnosis below).

The *typhoid* form occurs in one of the two following variants: it may begin with manifestations of general intoxication resembling the typhoid state, or, setting in with a clinical picture of acute salmonellal gastroenteritis involving a high temperature reaction it exhibits a 2-3-day remission with subsequent development of the typhoid state. These cases show a saddleback temperature curve, each wave lasting 5-6 days. The causative agents circulate in the blood all through the febrile period and produce stable bacteraemia. Many sporadic cases and outbreaks have been described. The typhoid course of food poisoning is observed mainly in cases of paratyphoid fever C; this disease is sometimes characterized by transition (although rarely) to protracted forms and may also develop chroniosepsis with formation of purulent foci in different organs and tissues.

Diagnosis. The main role in diagnosing food poisoning is played by the clinical picture of the disease and the epidemiological data (the connection of the given case with consumption of an infected food) supplemented by bacteriological and serological tests; the diagnosis requires cultures of the stool, blood, vomitus and the gastric lavage waters in Ploskiryov's medium. An agglutination test of a water suspension or homologous strain with the patient's blood serum may be performed as early as the 8th-10th days of the disease. The test should be repeated every 4-6 days, taking note of the increase in titres.

A *differential diagnosis* should be established in cases of acute poisoning with mushrooms and chemical substances, paratyphoid fever B, cholera and dysentery; the epidemiological data must be taken into consideration. It should be remembered that in cholera diarrhoea precedes vomiting, there is a sharper dehydration, and convulsions are often observed; if cholera is suspected, it is necessary to consider the epidemiological data and make cultures of the patient's stool and vomitus in 1 per cent peptone water (see Table 1).

Cases of the *gastroenterocolitic* form of food poisoning require a differential diagnosis with acute dysentery which, especially when caused by Sonne's bacilli, may in its course resemble salmonellosis. It should be remembered that in dysentery pains are more frequently observed in the region of the sigmoid colon and the lower part of the abdomen, a spasm of the sigmoid colon is noted more

often and is more strongly pronounced, the stool not infrequently contains mucus and blood, and rectoromanoscopic data attest more distinct changes in the mucosa of the colon.

Patients suffering from food poisoning of salmonellal aetiology have diffuse abdominal pains and leucocytosis, and vomit repeatedly.

To draw a clear line between acute dysentery and food poisoning, it is necessary to make wider use of bacteriological and serological tests. It should be remembered that myocardial infarction may be accompanied by symptoms resembling those of food poisoning.

If food poisoning is suspected, it is necessary to perform bacteriological tests of the faeces, vomitus and gastric lavage waters collected from the patient (separately!) in sterilized glass jars with tight-fitting lids.

In addition to the above, it is necessary to test bacteriologically the foods which served as the cause of the poisoning. In winter the jars with the samples are transported to the laboratory in a box padded with cotton. About 150-200 g of vomitus, a similar amount of gastric lavage waters and 200-250 g of the suspicious food consumed by the patient are sent to the microbiological laboratory to be tested. Each of these samples is taken in a clean and preliminarily sterilized glass jar tightly covered with oil-paper.

Treatment and care of patients. Immediately after admission of the patient to the hospital it is necessary to wash out his stomach through a thick tube with a warm 0.5 per cent sodium bicarbonate solution. At the same time the patient is given a salt cathartic (25 g of magnesium sulphate). It is important to watch the state of the cardiovascular system and systematically to control the blood pressure, resorting, if need be, to ephedrine, cordiamine and even to mesaton (meta-oxyphenyl methylaminoethanol hydrochloride). In cases of marked intoxication the patient is administered twice a day intravenously 0.85 per cent physiologic saline solution—500 ml for each infusion and additionally 2 litres a day by the drip method. Simultaneously physiologic solution and a 5 per cent glucose solution (500 ml each) are administered subcutaneously into the lateral surface of the thighs. In addition to the infusions of physiologic solution the patient is daily given a 40 per cent glucose solution (50-100 ml per infusion) intravenously. In cases of extreme dehydration of the organism the patient is administered, in addition to the foregoing, 15 ml of a 10 per cent sodium chloride solution once or twice a day intravenously; massive drip infusions of a 5 per cent glucose solution are beneficial.

Antibiotics do not decide the success of the treatment, but levomycetin may be recommended in a dose of 0.5 g 6 times per day for 4-5 days (although the therapeutic effect is very doubtful). The patient must be kept in bed; in cases of circulatory disorders hot water bottles are applied to the feet. A sparing diet is required for the period of acute manifestations of the disease.

In a state of collapse the patient must be given an infusion of freshly prepared Polosukhin's antishock solution (500 ml) and physiologic solution; vascular tone is maintained by injections of ephedrine or cordiamine and sometimes mesaton.

The patient's excrements must be disinfected directly in the bedpan with a 10 per cent clarifying chloride of lime solution in an amount equal to that of the excrements. Convalescents are discharged after clinical cure on the basis of negative results of their stool culture.

Prevention. The main part in preventing food poisoning is played by veterinary and sanitary control of cattle to be slaughtered, observance of the rules of sanitation and hygiene in storing meat, fish and other foodstuffs, and proper processing and storing of food under refrigeration.

All tables and boards on which food is dressed, as well as all other kitchen accessories, must be kept clean. Workers of the food industry, kitchens, children's institutions, restaurants, food shops and stalls must observe the rules of sanitation and hygiene in dressing and storing foods under refrigeration and must see to it that the consumers get high-quality fresh foodstuffs. They must make sure that their hands are always clean and that they are not affected with pyodermas since contamination of foodstuffs with purulent discharges from the skin of the hands may lead to severe streptococcus and staphylococcus food infection.

Veterinary and sanitary-hygienic control must be effected daily at places designed for cattle slaughter and carcass-dressing, as well as for fish-salting. Some kinds of fish, particularly humpback salmon, may, when salted under unsanitary conditions, become infected with salmonellae, for example, *Gärtner's* bacilli.

Scientifically elaborated rules of food hygiene are now observed and methods of bacteriological and serological control of meat, fish and milk are widely used in the USSR.

BOTULISM (BOTULISMUS)

Botulism is an acute general infectious disease of the group of food poisoning; it is caused by the *Clostridium botulinum* (an anaerobic bacillus) and is characterized by severe focal toxic affection of the central nervous system.

Aetiology. The causative agent of the disease is the strictly anaerobic and spore-bearing bacterium *Clostridium botulinum* which is capable of secreting, both in pure cultures and in the infected organism, one of the strongest poisons (exotoxin) whose pathogenic effect is greater than that of any other known bacterial exotoxin. Its pure exotoxin has been produced in crystalline form.

Five types of *Clostridium botulinum*—A, B, C, D and E— are distinguished according to their antigenic properties and formation

of exotoxic substances. The cases of botulism described in the USSR were caused by the A, B and E types.

As strictly anaerobic microorganisms the causative agents of botulism very well develop in foodstuffs which have little access of air.

Smoked and salt meats (especially ham and sausages), some kinds of cartilaginous fish, canned meat, fish and vegetables may be infected with vegetative forms or spores of the *Clostridium botulinum*. In the external environment the causative agent of the disease exists mainly in the form of spores noted for considerable resistance to various unfavourable external influences.

The vegetative forms of the *Clostridium botulinum* produce especially virulent exotoxins. The guinea pig can be killed by intraperitoneal administration of 0.000.001 ml of liquid botulinus toxin.

Epidemiology. Botulism may occur in sporadic cases and in small outbreaks; the latter is due to consumption of the same infected food by several people.

Botulism is usually caused by consumption of foodstuffs containing botulinus bacteria (vegetative forms and spores), as well as the exotoxin produced by the causative agent. The exotoxin forms the most intensively at a temperature of 35-37°C.

Ham, sausages, canned meat, fish and vegetables and cartilaginous fish (sturgeon, beluga, sevryuga) are most commonly infected.

Botulinus bacteria are rather widely distributed in nature and are found on vegetables, fruit, grain and fodder grasses. Cartilaginous fish becomes infected if it is damaged when caught or dressed, the botulinus bacteria penetrating from the intestinal contents of the fish where they may be present under normal conditions. Fish freshly dry-cured at home and home-made canned foods and ham may constitute a serious epidemiological danger.

To prevent the possible infection of cartilaginous fish and sprats where they are caught, dressed and canned, it is necessary strictly to observe the requisite sanitary and hygienic rules. At canning factories both the raw materials and the containers must be kept under hygienic conditions. All foodstuffs at storehouses, provision shops, public catering establishments and at home must be kept under refrigeration.

In some cases it is possible to determine the infection of ham and sausage with botulinus bacteria by the peculiar odour of rancid oil. It is characteristic that separate parts of meat and fish products may become infected with the result that some of the people who have consumed the given product may contract the disease, while the others remain well.

Pathogenesis. Botulinus bacteria (vegetative forms and spores which germinate in the intestines) and their exotoxin may gain entrance into man's gastrointestinal tract together with infected food. Soon afterwards the bacteria penetrate into the general cir-

culatation. Absorbed through the intestinal wall the exotoxin also passes into the general circulation. The toxin affects mainly the cells of the cranial nerve nuclei and causes diffuse changes in the ganglionic cells of the central nervous system. The bacterial invasion through the intestinal wall gives rise to temporary bacteraemia with subsequent implantation of the causative agent in the tissues and organs.

It should be emphasized that, unlike many other bacterial exotoxins, the toxin produced by the *Clostridium botulinum* is not destroyed by the action of gastric and intestinal juices.

The most characteristic results of intoxication are pareses and paralyzes of pharyngeal and oculomotor muscles, vagal paresis and injury to nerve ganglia of the heart.

Histological examination of the brain of people who died of botulism reveals grave degenerative changes in the ganglionic cells, circulatory stases and capillary haemorrhages. The myocardium is affected by a diffuse dystrophic process. Various parenchymatous organs exhibit dystrophy of cells and tissues, and botulinus bacteria are often found in the tissues.

Clinical picture. The incubation period is 6-10 hours, but may last as long as 48 hours. The disease sets in acutely with a headache, general indisposition, weakness and sometimes repeated vomiting. The stool is in most cases retarded and the abdomen is inflated (meteorism). The temperature rises insignificantly and but for a short time. From one to two days after the onset of the disease the patient begins to experience giddiness and develops photoperception disturbances, i.e., sees all objects as though in a mist; this sensation is followed by *diplopia* (double vision) which is due to paresis of associated movements of the eyes (convergence disorder); the pupils are dilated, one pupil often being wider than the other (anisocoria), marked strabismus appears, the upper eyelid droops (ptosis) and accommodation of the pupils to light is absent.

The patient's speech becomes inarticulate (dysarthria) and the voice weak; deglutition is disturbed and the patient chokes, experiencing difficulties in swallowing not only solid, but also semiliquid food (dysphagia).

The oral mucosa is dry and the patient is discomforted by thirst. The pulse lags behind the temperature level; later cardiac activity is affected. The borders of the heart are somewhat extended, the apical sounds are dull, and a systolic murmur is sometimes auscultated. The cardiac disturbances may persist for a long time. The capillaries become more fragile. In severe cases and in the absence of treatment or in cases of untimely treatment the patient may die as the result of bulbar paralyzes (with affection of the medulla oblongata nuclei and the ninth and tenth pairs of cranial nerves) and extreme cardiac failure.

The disease lasts a total of 4-15 days.

Diagnosis. The disease is diagnosed on the basis of the clinical picture and epidemiological data, i.e., consumption of infected food, and, in case of an outbreak of botulism, other patients who consumed the same food.

The following biological test may be performed to confirm the clinical diagnosis: 9 ml of blood is taken from the patient's ulnar vein into a test-tube containing 1 ml of a 4 per cent sodium citrate solution; 2 ml of this citrated blood containing the exotoxin of botulinus bacteria is administered intraperitoneally to each of 3 white mice of which two must die 4-7 hours after the injection; the third mouse is used as control (it is preliminarily administered 500 U of polyvalent antitoxic serum).

The meat and fish suspected of infection with the *Clostridium botulinum* is forwarded (in large quantities—400-500 g) to a laboratory, each portion in a clean, dry and preliminarily sterilized (by boiling) glass jar covered with oil-paper, sealed and properly labelled.

To test fish, parts adjacent to the spine, and internal organs are used. In choosing fruit and vegetables to be tested for infection with botulinus bacteria parts with dark spots should be taken. Canned foods must not be tested for botulinus bacteria and their exotoxin before the jars have been kept in a thermostat for 10-12 days; the contents to be tested must be taken from the internal layers of the cans and fed to 3-4 white mice which die within 22-30 hours, if the food contains botulinus exotoxin.

Botulism must be *differentiated* from other forms of food poisoning, bulbar forms of poliomyelitis and rabies, and tick-borne and lethargic encephalitis in the first 3-4 days of these diseases. It should be emphasized that diplopia is the earliest and most typical symptom of botulism; for timely revealment of this symptom the method of examining the patient described below is recommended.

The patient's head is fixed in a definite position and a red glass is placed before one of his eyes so that he may look through it at a lighted candle located along the patient's midline at a distance of 1.5 m from the face (Fig. 20).

In the presence of even feebly marked diplopia due to weakness (paresis) of one of the oculomotor muscles the patient will see two differently-coloured images of the candle. The eye behind the red glass will see the candle flame as red and the naked eye will see it as usual. This simple test makes possible early detection of the symptom of diplopia, which facilitates the diagnosis of botulism and ensures timely administration of antitoxic therapy.

Treatment. As soon as possible after admission of the patient to the hospital or even at a polyclinic or dispensary the patient must be given a gastric lavage with a warm 5 per cent sodium bicarbonate solution and administered 25 g of magnesium sulphate per os.

Treatment with antibotulinus serum should be started as early as possible; by periodically renewing its stock in every hospital it is possible to ensure timely treatment for every botulism patient.

Before administration of the prescribed amount of antitoxic serum the patient's organism is desensitized with small doses of it. A polyvalent serum containing A, B and E antitoxic serums is used for the treatment.



Fig. 29. Examination for dysphagia during the initial period of therapy.

An average of 150,000 U of polyvalent serum (containing 50,000 U of types A, B and E each) is administered on the first day. The dose may be increased in accordance with the severity and duration of the disease.

During the following two days the serum is administered in the same doses and then for another 2-3 days in somewhat smaller doses. It is best to administer the serum *intramuscularly*. The *paralytic* effect is achieved by the first administration of the serum (for greater detail see "Principal Methods of Treating Infectious Patients," General Information).

Treatment with antitoxic serum leads to rather rapid disappearance of the morbid symptoms, but it has to be supplemented with subcutaneous infusions of physiologic solution or intravenous drip infusions of a 5 per cent glucose solution and administration of cardiovascular agents (ephedrine, cordiamine and camphor strictly according to indications).

Owing to the *deglutition disorder* botulism patients have to be fed through a tube (see Fig. 10) and nutrient enemas. Persistent constipation is eliminated by high enemas. The patient may be allowed out of bed only after disappearance of all morbid cardiac symptoms.

To enhance the immune reaction of the organism and its desensitization to the botulinus toxin, it is recommended that patients should be administered botulinus *anatoxin* in addition to the anti-toxic serum. The anatoxin is administered intramuscularly in a dose of 0.5 ml of each type (A, B and E) of anatoxin for the first injection and similar doses of these types of anatoxin once more 5 days later.

Prevention. The principal role in preventing this disease is played by social prophylaxis—systematic sanitary control of the food, particularly the canning, industry, the meat and fish trade, and proper storage of perishable foods. If the can is inflated food it contains must not be consumed. To control the quality of canned foods, the latter must be selectively examined bacteriologically in provision storehouses, food shops and public catering establishments.

Personal prevention consists in consuming only fresh, high quality foods, especially ham, sausages and canned foods. Consumption of freshly salted fish, including cartilaginous fish, prepared by home methods must be avoided. Boiling of frying meat and fish in small portions prevents infection with botulism.

DYSENTERY (DYSENTERIA)

Dysentery is an infectious disease which spreads epidemically upon infection of man through the digestive tract; it is characterized by general intoxication of the organism, anatomical and functional affections of the large intestine, and frequent liquid stool containing mucus and blood.

Acute and chronic forms of dysentery are distinguished.

Brief historical information. The writings of ancient physicians which have come down to our time contain descriptions of acute human gastrointestinal diseases resembling dysentery. The disease was very clearly described clinically already in the 17th century. In the first half of last century physicians were quite familiar with the clinical course and pathologic anatomy of the "bloody flux"; but the disease was clearly distinguished from the similar disease—amoebiasis—by N. S. Solov'yov (Tomsk) only at the very end of the 19th century after it had been discovered that the disease was caused by bacteria. The causative agent of dysentery—*Bacillus dysenteriae*—was for the first time described by A. V. Grigoryev in 1894 and in much greater detail by the Japanese investigator K. Shiga in 1898; the latter had studied a number of important biological properties of this bacillus. Other types of causative agents of this disease were described later.

Until 1940 dysentery, whose causative agents then most commonly belonged to toxigenic types of bacteria, was, in addition to symptomatic agents, widely treated with antitoxic serum; later this serum was replaced by sulphonamides, but today it is extensively treated with synthomycin, levomycetin, streptomycin, biomycin and other antibiotics.

Actiology. Dysentery may be caused by various species of dysenteric bacteria; these includes the Grigoryev-Shiga bacteria, Flexner's bacilli, Sonne's bacilli, Newcastle's bacilli, etc. Morphologically all representatives of this group of bacteria are 3- μ -long nonmotile, gram-negative rods with rounded ends. The Grigoryev-

Shiga bacteria are capable of producing a virulent exotoxin. The most common causative agents of dysentery today are Flexner's and Sonne's bacilli (of several serotypes) and from time to time — Newcastle's bacilli, whereas Grigoryev-Shiga's bacteria are hardly ever isolated from the stool of dysentery patients.

The bacilli dysenteriae are very sensitive to heat and cold and various disinfectants (10 per cent chloride of lime, 2 per cent chloramine solution, 3 per cent lysol solution, etc.). In the external environment (excrements or underwear soiled with faeces) dysenteric bacteria may remain viable for a long time at a temperature of 18-25°C. At high temperature of the air, under the action of direct sunlight and on desiccation they quickly die. In moist soil and in cesspools at a temperature of 5-15°C they may live for 1.5-2 months. In milk and dairy products and on the surface of fruit, berries and vegetables they retain their viability for close to 2 weeks. They may remain alive for the same period of time on the surface of paper and metal money contaminated with faeces. Heating to 60 C and the action of a 1 per cent carbolic acid solution kill them in 25-30 minutes.

Dysenteric bacteria possess enzymatic activity, i.e., they split monosaccharides; this circumstance is utilized for purposes of laboratory diagnosis. They may acquire resistance to drugs and are readily cultivated in artificial nutrient media—agar and Ploskiyov's medium. Extensive biological variability of the causative agents of dysentery—formation of atypical L forms and filtrable forms of bacteria—has now been demonstrated.

Epidemiology. The sources of infection under natural conditions are human beings affected with acute and chronic dysentery, and bacteria carriers. The carrying of the infection is usually combined with chronic dysentery which now and then produces relapses. Dysenteric bacteria are discharged into the external environment in the faeces of patients and carriers.

Human beings are infected as the result of penetration of dysenteric bacteria into the gastrointestinal tract through the mouth. The causative agent localizes in the folds of the mucosa of the lower portion of the large intestine. The inoculation of human beings may occur primarily through contaminated hands, most commonly through various things infected by the excrements of dysentery patients or carriers. The disease no less frequently sets in as the result of consumption of water, milk and foodstuffs infected with dysenteric bacteria. A certain role in spreading dysentery is also played by flies.

Cases of dysentery occur all year round, but their greatest incidence falls on July and August, which is due to more frequent consumption during this period of unwashed raw vegetables and fruit, drinking of raw water, and partly to greater multiplication and activity of flies.

Failure to observe rules of personal hygiene plays a very important role in the epidemiology of dysentery. Serious importance in the epidemiology is attached to patients with atypical and obliterated forms of acute dysentery, patients with chronic dysentery and bacteria carriers.

Pathogenesis and pathologic anatomy. Gaining entrance into the digestive tract through the mouth, dysenteric bacteria localize in the lower portion of the large intestine, mainly in the folds of the mucous membrane. The pathologic changes in the lower portion of the large intestine, mainly in the sigmoid colon and the rectum, including its sphincter, are due primarily to the direct action of the toxic products (endotoxins or exotoxins) of the bacteria on the mucous membrane. Moreover, the mucosa is affected by liberation of the toxic substances, absorbed by the blood, back into the lumen of the intestine through the same portions of the mucosa.

In evaluating the role played in the pathogenesis of dysentery by the intoxication of the organism with the toxic products of the causative agents (exo- and endotoxins) it must be assumed that the principal role is played by lesions in the cardiovascular and nervous systems, salt and water metabolism disorders, and the injurious action of the toxins on the mucosa of the large intestine.

The anatomic changes in the mucosa are manifested in development of catarrhal, haemorrhagic, fibrinous and ulcerative processes. The character of the changes in the mucosa of the large intestine during the different stages of the disease may be traced by repeated examinations of the lower portion of the large intestine with the

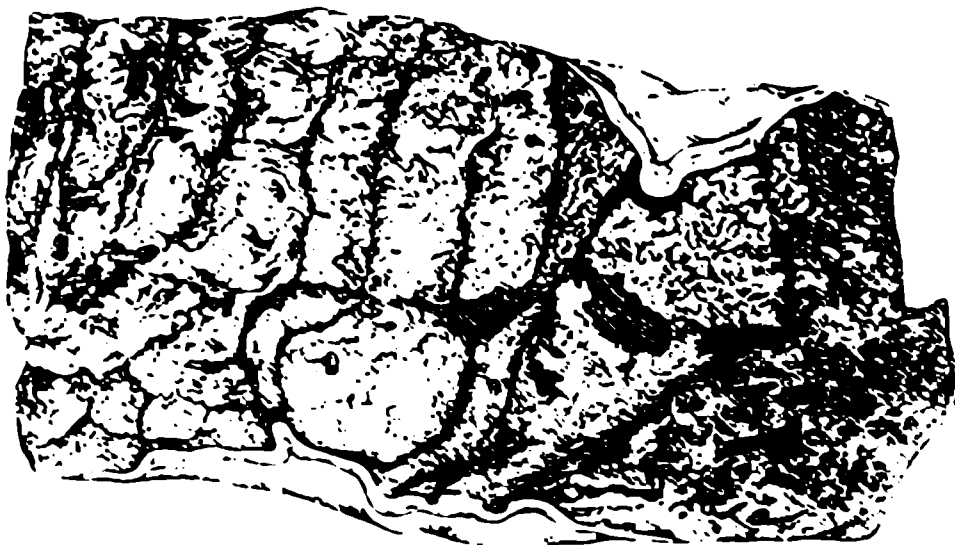


Fig. 21. Acute dysentery. Ulcerous (diphtheritic) inflammation of the large intestine (5th day of the disease).

aid of a special optic instrument (rectoromanoscope). In cases of death from severe forms of dysentery, which are extremely rare today, the changes in the mucosa of the large intestine may be discovered on the dissecting table and by pathohistological examination.

Today the dysentery caused by the Flexner, Sonne and Newcastle strains of bacteria, which secrete no exotoxin, most commonly exhibits catarrhal and catarrhal-haemorrhagic processes and much less frequently erosive and fibrinous-ulcerative changes in the mucosa (Fig. 21). These changes are found mainly in the region of the sphincter of the rectum, but they may occur all along the rectum and in the sigmoid colon.

The intoxication of the organism by the endotoxins of the causative agent of dysentery is responsible for the disturbances in normal activity of the nervous and cardiovascular systems and the metabolic disorders. The water, salt, protein and vitamin metabolism, and to a lesser extent carbohydrate and fat metabolism, are altered. Thus the most important clinical manifestations of the disease are determined by the injurious influence of the toxins of dysenteric bacteria on the organs and tissues. Pathohistologic examinations in severe toxic cases ending in the patient's death reveal signs of injury to the cells of sympathetic nerve ganglia, ganglionic cells of the cerebral cortex and of the myenteric and submucous plexuses. At the same time degenerative changes are found in various parenchymatous organs (liver, spleen).

The development of intoxication also involves metabolic disorders in the organism of the dysentery patient manifested primarily in disturbances of the water-salt balance.

Dysentery is accompanied by development of mild and unstable immunity of a monospecific character. This explains the possibility of repeated infections (reinfections) caused by other species of dysenteric bacteria. In view of the aforesaid characteristics of immunity in dysentery, specific prevention (vaccination) cannot ensure an appreciable decrease in the incidence of the disease among those subjected to vaccination.

Clinical picture. The incubation period averages 3 days with possible fluctuations from 2 to 6 days. Below is a description of a typical moderately severe case of dysentery caused by Flexner's bacilli.

The development of the acute phenomena of the disease is not infrequently preceded by a prodromal period (general weakness, indisposition, loss of appetite); this is followed by a rise in temperature, abdominal pain localized mainly in the left iliac region and frequent liquid stool of a faecal character. Within a few hours, or on the next day, the stool becomes still more frequent and contains free, i.e., unmixed with the faeces, mucus and streaks of blood; in some cases there may be a lot of mucus and small clots of blood.

Owing to the spasm of the lower portion of the large intestine the patient develops tenesmus (painful straining to empty the bowels), the stool becomes scant, quickly loses its faecal character and consists for the most part of mucus with an admixture of blood and sometimes even pus; often it is only a small clump of mucus with streaks of blood. With frequent tenesmus the anus appears pliant under pressure and sometimes gaping. The patient may have 20-25 bowel movements a day, but during the first 2 days most patients have 10-12 a day. As the patient begins to recover, he defaecates less frequently.

Palpation of the abdomen in the left iliac region reveals a spasm and extreme painfulness of the sigmoid colon which is palpated as a dense cord. The tongue is usually coated with a white film. The patients often feel cold because of the disturbance in the water-salt metabolism. The temperature may rise high ($38.5-40.5^{\circ}\text{C}$), but the fever does not last long—2-4 days. These cases are accompanied by moderate intoxication, and rectoromanoscopy reveals catarrhal or catarrhal-haemorrhagic proctosigmoiditis. The blood picture is not characteristic.

As the patient begins to recover, his general condition improves, his bowel movements become less frequent and the stool contains neither mucus nor blood. From 9 to 10 days after the onset of the disease the stool becomes pultaceous and then gradually normal.

To evaluate the clinical treatment of dysentery, it is necessary to take into account the degree of intoxication (1st, 2nd and 3rd degrees), the characteristics of the stool (frequency, presence of admixtures), spasm of the sigmoid colon and the character of anatomic changes in the mucosa of the large intestine revealed by rectoromanoscopy.

Besides the afore-described form of the disease there are also severe toxic cases. Toxic cases of dysentery are characterized by a sharp depression of the nervous system, to the point of prostration and convulsions, and considerable disorders of the cardiovascular function sometimes resulting in death. These are fulminant cases of the disease particularly attacking small children.

The severe general intoxication of the organism may be accompanied by such sharp cardiovascular insufficiency and depression of the nervous system that the liquid stool and tenesmus become manifest only several hours after the development of general symptoms. Toxic dysentery usually caused by Grigoryev-Shiga's bacilli (this form now occurs very rarely) is characterized by tenesmus, 30-50 bowel movements a day (very thin stool with mucus and blood), dehydration of the organism and intoxication.

In present-day cases of dysentery the blood pressure usually drops moderately and some patients exhibit clinical and electrocardiographic signs of myocardial dystrophy.

Gastric secretion and intestinal secretion of enzymes are often

disturbed. The immune reactions of the organism are depressed and the composition of the normal bacterial flora of the intestines is altered.

Concurrent helminthiasis (for example, ascariasis) or the presence of protozoans (trichomonads) considerably aggravate the course of dysentery and are conducive to development of its protracted and chronic forms.

The special feature of dysentery caused by Sonne's bacilli is that the pain and spasm of the large intestine may be observed in the region of the transverse and ascending colon and even the caecum. Sonne's dysentery is characterized by an acute onset, often with chills, vomiting and pains in the right half of the abdomen. Some cases show considerable resemblance to food poisoning. These characteristics of Sonne's dysentery must be taken into consideration in establishing the diagnosis since in some cases the disease was erroneously diagnosed at the onset as food poisoning or acute appendicitis.

Cases of dysentery caused by Newcastle's bacilli are characterized by an acute onset, rapid rise in temperature up to 39-39.5 C, nausea, vomiting, and paroxysmal abdominal pains. A frequent liquid stool containing mucus and sometimes streaks of blood appears on only the second day (and in some cases on the 3rd day) of the disease.

In the presence of chronic anacidic gastritis and in persons suffering from alimentary dystrophy and avitaminosis acute dysentery not infrequently runs a protracted course owing to the low reactivity of the organism and the depression of its protective mechanisms.

Development of protracted forms of dysentery is fostered by such factors as failure to keep to a diet, occupational intoxications, and early discontinuance of treatment with antibiotics or sulphonamides.

Present-day course of the disease. In the last ten years the disease has been observed to run a milder course which is due to the increased resistance of the population to the disease, improvement of nutrition and replacement of the toxigenic species of causative agents of dysentery—the Grigoryev-Shiga bacilli—by the less virulent Flexner's, Sonne's and other species. Severe forms of the disease with sharp intoxication, tenesmus and considerable affection of the mucosa of the large intestine are now observed relatively rarely. There are *atypical* forms accompanied by a moderate spastic pain and haemocolitic syndrome and slight intoxication. These forms require careful differential diagnosis primarily with food poisoning of salmonellal aetiology.

Clinical aspects of dysentery in early childhood. Clearly marked phenomena of secondary toxicosis with an insufficiently clear haemocolitic syndrome are characteristic of children during the first two years of life. The stool is rather rarely observed to contain

blood. Despite the continuous presence of mucus the liquid stool of infants affected with acute dysentery often retains its faecal character and assumes a greenish colouring. The abdomen is inflated, paresis of the sphincter ani is often observed, and tenesmus occurs infrequently. Considerable dehydration of the organism, anorexia, emaciation of the infant and a protracted course of the disease supplement the clinical picture. In infants of the first year of life dysentery may be combined with coli-dyspepsia (mixed infection) which leads to considerable aggravation of the patient's condition and development of a chronic affection of the gastrointestinal tract.

In most cases acute dysentery ends in complete cure, especially with early and proper treatment, including bed rest and appropriate diet; however, in some patients dysentery may last 3-4 months (protracted dysentery) with early or late relapses.

Some cases, especially in persons who have survived acute dysentery caused by Flexner's bacilli, may give rise to *chronic recurrent dysentery*. Formation of chronic dysentery is fostered by helminthiases and protozoan invasion, failure to keep to one's bed and to the prescribed diet during the acute period of the disease, inadequate treatment of acute dysentery, chronic (including occupational) intoxications, insufficient immune reaction in debilitated patients, and a number of other factors.

From time to time a *continuous* form of chronic dysentery with no remissions is observed.

Chronic recurrent dysentery is characterized by aggravations which last 2-4 weeks and alternate with remissions lasting several months. Chronic dysentery may last a few years, the chronic patients constituting a danger as sources of infection. An unstable stool and frequent aggravations discomfort the patients and temporarily incapacitate them. A protracted course of chronic dysentery unfavourably affects the patients' general condition and evokes many subjective disorders—unstable mood, poor sleep, abdominal pains and pathologic stool.

In younger children the course of acute dysentery is characterized by a number of special features—frequency of severe forms (in some cases with marked intoxication and dehydration), frequent stool with an abundance of mucus and slow normalization of the stool. Moreover, children are particularly inclined to develop protracted forms of the disease with the stool long containing the causative agent.

Diagnosis. The diagnosis of dysentery requires a careful analysis of epidemiological data and of the entire clinical picture of the disease with the use of laboratory methods. Ascertainment of the diagnosis is facilitated by examination of the lower portion (25-30 cm) of the large intestine with the aid of a rectoromanoscope which is an optic instrument with a metal tube and a bulb intro-

duced into the rectum and the sigmoid flexure. The first rectoromanoscopic examination is resorted to after disappearance of the most acute phenomena; it is repeated 3-4 days later.

It should be emphasized that rectoromanoscopy does not yield any picture specific of dysentery, but serves as certain confirmation of the diagnosis just the same.

The most authentic laboratory confirmation of the diagnosis is isolation of dysenteric bacteria from the patient's stool, for which reason the warm faeces from the bedpan are inoculated in Ploski-ryov's medium or in Petri dishes containing agar. If the inoculation cannot be made at the patient's bedside, the faeces are taken into a test-tube containing a conserving mixture (magnesium sulphate solution with glycerin). At the same time it is necessary to make a culture of faeces taken from the patient's rectum with a thin glass rod having rounded edges and a culture of the enema water from a rectal and sigmoid microclyster. The laboratory gives the preliminary answer as to whether there is a growth of dysenteric bacteria within one day and the final answer (indicating the species of bacteria) within 3 days.

Examination of the dysentery patient's faeces may reveal an increase in leucocytes and erythrocytes, the presence of mucus and columnar epithelium.

An agglutination test is performed at a later period of the disease (after the 10th or 11th day); the patient's blood serum diluted with physiologic solution agglutinates dysenteric bacteria. A 1 : 200 and greater dilution of the serum is taken as the diagnostic titre of the test; on repeated tests of the patients' blood serum the titre increases. This method may also be used to diagnose *chronic dysentery*, which is particularly important in cases unconfirmed bacteriologically.

In establishing a *differential diagnosis* it is necessary to consider food poisoning, protozoan and toxic colitides and, in some cases, also the possibility of polyps and cancer of the rectum (revealed rectoromanoscopically). In view of the considerable resemblance of the clinical manifestations of acute dysentery to those of a number of other diseases, differential diagnosis not infrequently presents great difficulties. *Alimentary enterocolitides* are diagnosed on the basis of the absence of marked general intoxication of the organism and spasm of the sigmoid colon.

Amoebiasis is, in addition to epidemiological data, characterized by right-sided colitis and the presence of a large amount of mucus in the patient's stool evenly coloured with blood and therefore resembling raspberry jelly; the question of diagnosis is decided by discovery of tissue forms of histological amoeba in natural or stained stool preparations.

Owing to the considerable resemblance of dysentery to *balantidiasis* the latter may be diagnosed only through a repeated and persistent search for balantidia in the stool.

Colitides of occupational origin (in persons having to do with mercury) are diagnosed on the basis of anamnestic data and the presence of mercurial stomatitis and symptoms of nephrosonephritis.

The clinical picture of *food poisoning* is characterized by a predominance of symptoms of acute gastroenteritis or gastroenterocolitis, but since the clinical course of these diseases resembles that of acute dysentery it is necessary repeatedly to perform bacteriological tests (see chapter "Food Poisoning") and from the 8th or 9th day of the disease to perform dynamic agglutination tests (with a water suspension and homologous strain).

Food poisoning usually begins with vomiting, once or repeatedly, and is followed by diffuse abdominal pains, frequent liquid stool and a rise in temperature; the liquid faecal stool, as a rule, contains no pathologic admixtures. Food poisoning caused by Breslau's bacteria is accompanied, as the result of bacteraemia, by elevated temperature and not infrequently typhoidlike intoxication which persists for several days. Repeated stool cultures in Ploskirvov's medium necessarily using a set of 15-18 type-specific (monoreceptor) agglutinating serums for identification, make it possible in a considerable number of cases to reveal causative agents of the poisoning belonging to the group of salmonellae.

Treatment and care of patients. In acute dysentery and during aggravations of chronic dysentery all patients must be hospitalized and confined to bed. A mechanically and chemically sparing diet is recommended. The diet consists of kefir, acidophyllin, sour milk, fresh curds, soft boiled eggs, white zwieback, small amounts of salmon (red) or sturgeon (black) caviare, 30 g of butter a day, mucilaginous oatmeal soup, soup with quenelles, steamed (during the first four days of the disease) meatballs, well-cooked rice and buckwheat groats, fresh boiled fish, jelly, mashed vegetables, ground and baked apples, fruit, berry and grape juices, oranges and tangerines. As the morbid phenomena abate the diet may be extended.

It is necessary to uncover and treat *concurrent helminthiases*; in the event of ascariasis oxygen therapy may be administered from the 6th or 7th day of the disease; later the patient may be given piperazine. Considerable importance is attached to saturating the organism with vitamins, to administering roborants and to compensating for the disturbed digestive functions (8 drops of diluted hydrochloric acid before meals in officinal prescription, and pancreatin in a dose of 1 g 3 times a day in the intervals between meals).

Antibiotics—levomycetin, biomycin, tetracycline and terramycin—are used for the treatment of acute dysentery and relapses of chronic dysentery. The treatment with any of the foregoing preparations lasts a total of 6-7 days; the duration of the treatment is based on its clinical effect. Vitamins are extensively used.

The *mean* therapeutic doses of antibiotics are 0.5 g 5 times a day

for levomycetin, and 300,000 U (which corresponds to 0.3 g of the preparation) 4 times a day for biomycin, tetracycline and terramycin. In addition to antibiotic treatment, vaccine therapy is recommended to stimulate the immune properties of the organism and to desensitize the latter. For these purposes an alcohol divaccine prepared by V. A. Chernokhvostov's method with Flexner-Sonne bacteria is administered subcutaneously in a dose of 0.5 ml on the first day, and 1 ml on the 3rd, 5th and 7th days. Dimedrol (diphenhydramine), diazoline (5-benzyl-1,2,3,4-tetrahydro-2-methyl-SH-pyridine-indole), diprozone (N-[2-dimethylaminopropyl] phenothiazine hydrochloride), pipalphen or suprastin are used for purposes of nonspecific desensitization of the organism.

Of all so-far suggested methods of treatment, practice has shown the following complex scheme of immune-antibiotic therapy proposed by K. V. Bunin in 1958 and extensively tested with good direct and long-term results in the clinic headed by the author to be the most effective.

Scheme of Immune-Antibiotic Therapy for Acute Dysentery
(K. V. Bunin, 1958)

Days of treatment	Biomycin or tetracycline per os 3 times a day in single doses of	V. A. Chernokhvostov's alcohol dysentery divaccine subcutaneously once a day in a dose of	Pentoxyl C-hydroxymethyl-2-methyl-thionaphthyl 3 times a day in a single dose of
1	0.3 g	0.5 ml	0.3 g
2	"	—	"
3	"	1 ml	"
4	"	—	"
5	"	1 ml	"
6	"	—	"
7	"	1 ml	"

This therapeutic scheme is recommended for extensive use in the treatment of acute Flexner-Sonne dysentery.

Sulphonamides—sulgine (sulphanilylguanidine), phthalazole (phthalylsulphathiazole) and disulphormin (1,4,4'-N-trimethylene-bis-[sulphanilyl-sulphanilamide]) may be used in the absence of antibiotics (1 g 4 times a day for 5-7 days); patients treated with these preparations are given plenty to drink.

In the treatment of *toxic forms of dysentery* it is necessary, in addition to antibiotics, to administer antitoxic antidysenteric serum (intramuscularly in a dose of 50,000-60,000 U per day for 2-3 days).

An individual approach to each patient is particularly important during *aggravation of chronic dysentery* since chronic dysentery usually involves complications and is combined with other processes (achylia, gastritides, helminthiasis, protozoan invasion, etc.).

After eliminating the acute phenomena (aggravation, relapse) it is necessary to treat the concurrent diseases.

During aggravation of chronic recurrent dysentery antibiotics are administered according to the same schemes as in the treatment of acute dysentery. In addition to this, Chernokhvostov's alcohol divaccine is administered every other day. It is injected subcutaneously, beginning with a dose of 0.2 ml on the first day of treatment, the dose being gradually increased on subsequent days to 2 ml by the tenth injection.

In addition to antibiotics and vaccine therapy in the treatment of chronic dysentery patients, the latter should be administered therapeutic enemas [camomile, colloid dispersed norsulfazol (sulphathiazole) salt, fish liver oil, 1 per cent tannin solution and vaseline oil to accelerate repair of the intestinal mucosa] and given general roborant treatment (glucose and vitamin therapy, blood, plasma and erythrocyte mass transfusions, and physiotherapy).

Schemes of treating children. The treatment of children affected with acute and chronic dysentery is based on the same principles as that of adults. However, special attention must be devoted to the patients' regimen and the patients must be ensured good care.

The following schemes are used in the treatment of acute dysentery:

(a) levomycetin—daily dose of 0.04 g (40 mg) per 1 kg of weight for children up to 3 years of age, and 0.8-1.2 g for children past 3 years of age;

(b) synthomycin—daily dose of 0.08 g (80 mg) per 1 kg of weight for children up to 3 years of age, and 1.2-2 g for children past 3 years of age;

(c) biomycin, tetracycline or streptomycin—daily dose of 20,000-25,000 U per 1 kg of weight for children up to 3 years of age, and 25,000-35,000 U for children past 3 years of age.

During treatment in a hospital the daily dose is divided into 4 intakes; for treatment of outpatients the daily dose may be divided into 3 intakes. The cycle of treatment lasts at least 7 days.

During the treatment of children affected with chronic dysentery it is necessary to uncover concurrent helminthiases and to dehelminthize the patients (after subsidence of the acute phenomena of dysentery). Nursery and kindergarten children affected with chronic dysentery should be organized in special groups.

Adults and children who have recovered from dysentery may be discharged from hospital on the condition that all clinical manifestations of the disease have disappeared and 2-3 stool cultures have yielded no dysenteric bacteria. Workers of the food industry, water-supply system, public catering establishments and children's institutions are subject to particularly careful bacteriological control upon discharge from hospital. Wherever bacteriological control is impossible the discharge must be based on clinical cure and the patients must be discharged between the 4th and 6th

days after normalization of the stool and must subsequently be kept under observation by their district dispensary; all persons who have survived dysentery must be kept under observation for a period of about 1 year.

In individual cases patients may be discharged after the 7th day of the disease, following the disappearance of clinical symptoms, but only on the condition that their therapeutic course will be completed by the district physician (or assistant physician) at home and in the gastrointestinal department of a dispensary, that the convalescents will subsequently be kept under observation and that due consideration is given to the sanitary conditions under which the convalescent will live after discharge. The treatment must be completed with an antibiotic other than that administered to the patient in the hospital. Those who have survived acute dysentery must in a number of cases take antirelapse treatment, the indication for which is protracted convalescence.

Prevention. Dysentery prevention is based on steady improvement of the sanitary state of populated areas and a rise in the cultural and material standards of the people. Rules of personal hygiene—hand-washing, washing of raw vegetables and fruit in boiled water before eating, drinking only boiled water and milk, etc.—must be strictly observed.

An important part is played by observance of the rules of food hygiene (storage of foods, their processing, delivery to the consumer and sale) and systematic control of flies—proper construction and cleaning of cesspools and dust bins, extermination of flies at the sites of their breeding by means of 10 per cent DDT, and in residential and industrial buildings by dusting with DDT and by means of flypaper.

All dysentery patients are subject to hospitalization. Patients may be left at home only in exceptional cases by permission of the district epidemiologist and only provided the sanitary conditions at home are satisfactory. Subsequent supervision of the focus is obligatory. Gastrointestinal departments of dispensaries and polyclinics must keep records of chronic dysentery patients and the latter must be treated during periods of aggravation of the disease.

Strict observance of all rules of hygiene is required in the surroundings of chronic dysentery patients. Final disinfection is performed at the focus after hospitalization of acute and chronic dysentery patients.

Chronic dysentery patients are not allowed to work in the food industry, restaurants, shops and children's institutions and are subject to observation by dispensaries.

Since preventive inoculation (enteral or subcutaneous vaccination) is still insufficiently effective, it plays no independent role and can only supplement the system of general preventive measures. At the present time there is no proof that any of the suggested

methods of vaccination are capable of producing direct effects, owing to which further inoculations against dysentery are considered inexpedient by most authors.

AMOEBIASIS

Amoebiasis is a disease caused by infection with *Endamoeba histolytica*; it consists in a predominant affection of the ascending colon and a discharge of mucosanguineous faeces, and is characterized by a tendency to a protracted and chronic course.

Aetiology. The causative agent of the disease is the *Endamoeba histolytica*, first discovered by F. A. Lesh (1875) in the excrements of an amoebiasis patient and described in detail by F. Schaudinn in Germany (1903). Two forms of *Endamoeba histolytica*—vegetative and encysted—are distinguished.

The vegetative form is in its turn divided into: (1) a *lumen* form (*Endamoeba histolytica forma minuta*) which lives in the upper portions of the colon and is the basic stage of the life cycle of the *Endamoeba histolytica*, and (2) a *tissue* form (*Endamoeba histolytica forma magna*) which parasitizes in the mucous and submucous coats of the wall of the colon of amoebiasis patients, where it produces deep ulcers.

The cysts of the *Endamoeba histolytica* form by successive transformations from the lumen form when the latter, moving along the intestinal tract, enters the lower portion of the colon where it is acted upon by products of putrefaction and fermentation. The diameter of the cysts ranges from 8 to 16 μ . They have a regular spherical form and are surrounded by a colourless membrane. A mature cyst contains 4 nuclei, while its protoplasm has a vacuole filled with glycogen. Excreted in the faeces of an amoebiasis patient the cysts may gain entrance into the gastrointestinal tract of a healthy susceptible person, where they are transformed into the lumen form of the *Endamoeba histolytica*. It should be noted that infection with the *Endamoeba histolytica* does not necessarily produce amoebiasis because only the implantation of its lumen forms in the wall of the colon and their subsequent transformation into tissue forms lead to the development of a clinically marked disease.

In cases of acute manifestations of the disease the mucosanguineous faeces of an amoebiasis patient contain tissue (*forma typica* Fig. 22) and lumen forms; as the process abates the faeces contain lumen forms and cysts; the faeces of healthy carriers also contain lumen forms and cysts. It should be emphasized that only the presence of the *tissue* forms of *Endamoeba histolytica* in the faeces being tested may serve as a laboratory confirmation of the diagnosis of amoebiasis.

The *lumen* form of *Endamoeba histolytica* lives mainly in the contents of the caecum of amoebiasis patients and carriers. Its

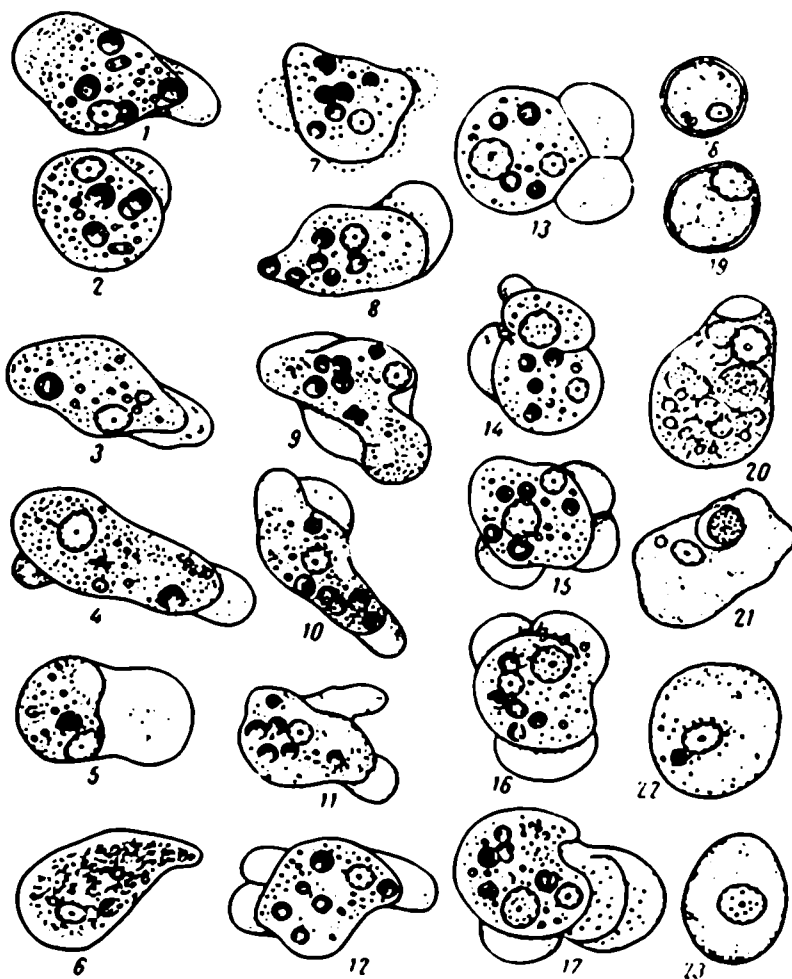


Fig. 22. Forms of development of the histolytic amoeba (1-23)

diameter reaches 12-25 μ . The amoeba has a spherical nucleus with clumps of chromatin evenly distributed in it.

In its lumen form the amoeba reproduces by simple division. The lumen form of *Endamoeba histolytica* is able to move by extending processes of protoplasm (pseudopodia) in front of the main part of its body.

Owing to the production of proteolytic ferments the lumen form of the amoeba is capable of causing dissolution (lysis) of tissues, hence the name of the amoeba as *histolytica*. As the result of destruction of the mucous and submucous coats deep ulcerous defects are formed in the wall of the colon. Penetrating into the wall of

the colon the lumen form enlarges (to 30-50 μ in diameter) and changes to the tissue form which plays the most important part in the pathogenesis of amoebiasis.

The tissue form contains phagocytized erythrocytes on which it feeds, causing destruction of the tissues in the wall of the colon. As the pathologic process abates, the tissue forms change to lumen forms and the latter, on entering the lower divisions of the colon, are capable of transforming into cysts.

The foregoing describes the life cycle of *Endamoeba histolytica*. Its structure is shown in Fig. 22.

Epidemiology. Healthy people become infected upon the entrance of mature (four-nucleus) cysts of *Endamoeba histolytica* into the gastrointestinal tract with subsequent formation of lumen and tissue forms and development of pathologic changes in the wall of the colon.

Carrying of dysenteric amoebae is widespread in various geographic areas and is not confined to the southern latitudes. However, clinically marked cases of amoebiasis are observed mainly in areas with a hot climate, but persons infected in these endemic areas may, upon moving to more northern latitudes, continue to have amoebiasis for a long time and sometimes become sources of new infection.

At the same time it should be emphasized that in addition to the excretion of dysenteric amoebae in the faeces of patients or carriers into the external environment, the spread of amoebiasis requires definite routes of transmission of this disease and certain factors increasing the susceptibility of the organism.

Epidemiologically the most dangerous amoebiasis patients are those with subacute and chronic forms of the disease and healthy carriers of *Endamoeba histolytica*.

The principal route of transmission is raw water polluted with the faeces of patients or carriers. Particularly dangerous is raw water from irrigation ditches.

Violation of the rules of personal hygiene, consumption of vegetables and berries from patches fertilized by undisinfected human faeces, and the use of foodstuffs and household utensils contaminated with cysts of *Endamoeba histolytica* may also lead to infection with amoebiasis. The considerable stability of cysts of *Endamoeba histolytica* in the external environment deserves special emphasis; at room temperature the cysts may retain their viability for 2 weeks in faeces, and for 8 months in water.

Pathogenesis and pathologic anatomy. Upon penetration into the gastrointestinal tract the cysts of *Endamoeba histolytica* lose their membrane under the action of pancreatic juice and change to the vegetative (lumen) form. The lumen forms of amoebae implant themselves in the wall of the colon and enlarge by changing to tissue forms.

The implantation of amoebae in the mucosa of the colon is made possible by the dissolution (lysis) of tissues under the action of proteolytic ferments produced by the lumen forms of amoebae. The dissolution of tissues results in formation of deep ulcerous defects in the wall of the colon. The ulcers are quite deep, their edges are loose and the floors are covered with pus and tissue detritus containing amoebae; the tissue around the ulcers is hyperaemic and its mucosa is oedematous. Folliculitides are often observed (Fig. 23).

The changes in the mucosa occur mainly in the caecum, the ascending and sigmoid colon and, considerably less frequently, in the rectum. The size, as well as the number and stage of development of the ulcers, may greatly vary, and there may be cicatrizing ulcers in addition to fresh ones. The diameter of the ulcers may be from 1 mm to 2-3 cm.

Spreading beyond the ulcers in the thick of the submucous coat of the intestine the tissue forms of *Endamoeba histolytica* may burrow passages in it, connecting separate ulcers.

The ulcers which penetrate deep into the wall of the colon may lead to perforation of the wall with resultant localized or generalized peritonitis. By penetrating into the intestinal vessels the tissue forms of *Endamoeba histolytica* may spread along the branches of the portal vein and cause an abscess in the liver. In some cases amoebae may be carried by the blood flow to the lungs or the brain where they may produce abscesses.

Clinical picture. The duration of the incubation period varies very widely and cannot be established with any degree of precision.

As a rule, the disease develops gradually. The prodromal period characterized by general indisposition, loss of appetite, mild abdominal pains, and nausea lasts from several hours to 1-2 days. It is followed by development of clinical symptoms of pathologic changes in the colon, typical of amoebiasis. The patient begins to have a frequent liquid stool of a faecal character with separate clumps of mucus. The amount of mucus in the stool increases, the mucus is sometimes evenly stained with blood, due to dissolution of the tissues by amoebae, and assumes the appearance and consistency of raspberry jelly. The stool may be 7-8 times a day and sometimes even more frequent.

The most common symptom of amoebiasis patients is alternation of an abundant diarrhoeal stool with mucous faeces. The patient is discomforted by paroxysmal abdominal pains which are due to spasms of various divisions of the colon. Defaecation is accompanied by an intense burning in the anal region.

Examination of the patient reveals a sunken abdomen and pain in the region of the caecum and ascending colon; these divisions of the intestinal tract are in a state of spasm.

Pain and spasm of the sigmoid colon are found less frequently.

which must be taken into consideration in *differentiating* the disease from dysentery. The febrile reaction is usually mild; from time to time subfebrility is observed. The organism is not intoxicated.

The patient is generally out of sorts and exhibits a poor appetite, insomnia and diminished working capacity—constant signs of the disease. The blood often shows eosinophilia and mild general leucocytosis; a protracted course of the disease leads to development of hypochromic anaemia. In severe cases the stool may look like meat slops, becomes fetid and occurs every hour or even more frequently; the patients become extremely emaciated and develop acute anaemia.

Rectoromanoscopy (mainly when the lesions are localized in the lower portion of the colon) reveals various changes—from superficial defects in the mucosa to large isolated ulcers with loose edges and floors covered with tissue detritus (Fig. 24).

Amoebiasis may persist for a very long time—many months and even years (chronic forms), with the result that the patients develop marked anaemia and cachexia. Because of the ulcerative process in the colon and the repeated, even if small, haemorrhages the patients' haemoglobin and erythrocytes sharply diminish.

Complications. The disease may become complicated by perforation of the wall of the colon in the region of the ulcer and by development of peritonitis. Sometimes there is an abscess in the liver (the dysenteric amoebae metastasize into the parenchyma of the liver from the intestinal wall along the portal vein system). As has already been mentioned, abscesses may develop in the lungs and the brain.

Diagnosis. The disease is diagnosed on the basis of epidemiological data and the clinical picture. The diagnosis is confirmed by discovery under the microscope of dysenteric amoebae (*Endamoeba histolytica*) in natural (unstained) preparations of the patient's faeces taken immediately after defaecation. The microscopy must be performed on a heating table or, if there is no such table, the preparation must be heated by an electric lamp located near the microscope. Sometimes, to discover amoebae in the patient's stool, preparations of mucus from the faeces stained with haematoxylin or a strong iodine solution are used (iodine—1 g, potassium iodide—2 g, distilled water—20 g).

It is necessary to have appropriate skills and use a special table—a classification key of amoebae—to be able to distinguish dysenteric amoebae from nonpathogenic amoebae, for example, *Endamoeba coli*. The most essential characteristic of the tissue form of *Endamoeba histolytica* is that it contains in its protoplasm engulfed erythrocytes.

Discovery of tissue forms of the amoeba in the patient's stool is of decisive importance to the diagnosis.

Differential diagnosis. The disease should be differentiated from

bacterial dysentery, and in acute forms of the disease—from food poisoning. Due consideration must be given to the clinical and epidemiological data and to the results of parasitological and bacteriological tests.

Treatment. For the period of acute manifestations of the disease and during relapses patients are subject to hospitalization and chemotherapy. The same diet is prescribed as for the treatment of dysentery (see "Dysentery").

The most effective treatment is that with emetine which is administered intramuscularly in the form of a 2 per cent water solution of emetine hydrochloride (*Emetinum hydrochloricum*) in a dose of 1.5-2 ml once a day for 7-8 days. In view of possible relapses 1-3 repeated courses of emetine treatment are additionally prescribed. Because of the possible toxic phenomena due to cumulation of the drug the repeated courses are administered at intervals of at least 6-8 days.

The daily doses of emetine hydrochloride for children must be: 0.005 g up to 1 year of age, 0.01 g from 1 to 2 years, 0.02 g from 2 to 5 years, 0.03 g from 5 to 9 years, and 0.04 g from 9 to 15 years of age.

Treatment with emetine produces good immediate results (rapid cessation of the mucosanguineous stool and of the spastic abdominal pains), but does not exclude the possibility of relapses. In virtue of this it is recommended, after beginning the treatment with injections of emetine, to combine this preparation, during repeated courses, with aminarsone (carbasone) according to the following scheme: in each of the repeated courses intramuscular injections of a 2 per cent emetine hydrochloride solution (3-3.6 ml per day) are given for the first 3 days and 0.25 g of aminarsone is given per os three times per day during the subsequent 5-6 days. During the entire treatment (in addition to the first, basic course of emetine injections) 1-3 combined courses of emetine and aminarsone are administered at intervals of 8-10 days. Usually this produces a good therapeutic effect and sharply reduces the frequency of relapses.

In cases complicated with an abscess of the liver emetine is supplemented with streptomycin and penicillin.

Entirely satisfactory results in the treatment of amoebiasis are produced by *biomycin* which is administered in a dose of 0.3 g four times per day for 5 days; after an interval of 6-7 days this course is repeated. Terramycin (0.3 g five times per day) is also effective.

Special attention should be devoted to roborant therapy: a therapeutic diet containing adequate nutritive substances and calories, saturation of the organism with vitamins, administration of arsenic, iron preparations and glycerophosphates, and in severe forms of the disease—repeated blood transfusions. Enemas with a 0.01 gram icidin solution (100 ml daily for 6-7 days) play a subsidiary role.

Prophylaxis. All patients with an acute or aggravated chronic

form of amoebiasis must be hospitalized and given systematic treatment.

Disappearance of the main clinical symptoms of the disease is the basic condition for the discharge from the hospital. Persons employed in food-processing enterprises, dining-rooms, lunch-rooms, restaurants, children's institutions, etc., are kept under medical observation after discharge from the hospital and their faeces are repeatedly tested for *Endamoeba histolytica*. As soon as they show the first signs of gastrointestinal disorders they are hospitalized, are carefully examined and are given chemotherapeutic treatment.

The faeces of persons of the above categories must be periodically tested for *Endamoeba histolytica*. If cysts of the amoeba are discovered in the faeces of a clinically healthy person, the latter is not dismissed from work and is treated as an outpatient with *yatren* which is administered per os in a dose of 0.5 g three times per day for 8-10 days; the same course of treatment is repeated after a 10-day interval.

Proper water supply and drinking only boiled water play an exceptionally important part in the control of amoebiasis. In addition to this, the rules of personal hygiene must be strictly observed, flies systematically exterminated, toilets permanently kept in good sanitary conditions and disinfected, and foodstuffs protected against contamination with cysts of *Endamoeba histolytica*. The faeces of patients must be disinfected by mixing with double the volume of 0.5 per cent lysol solution; it takes 20-25 minutes to disinfect them.

ASIATIC CHOLERA

Cholera is a particularly dangerous infectious disease characterized by an epidemic spread, sharp dehydration and intoxication of the organism, severe affection of the gastrointestinal tract, vomiting, frequent watery stool, drop in temperature, muscular cramps and haemodynamic disorders.

Actiology. The causative agent of cholera (*Vibrio comma*) was discovered by R. Koch in 1883. In stained pure culture preparations under the microscope it looks like a short, curved rod resembling a comma. At one end the *Vibrio comma* has flagella, owing to which it is capable of active movement. In the external environment it may retain its viability and motility for 3-4 days; it is destroyed by heat (above 15°C), direct sunlight, desiccation and disinfectants. At low temperatures and, especially, in water it remains viable for 3 weeks. *Cholera-like* vibrios nonpathogenic to man, but morphologically resembling the *Vibrio comma*, are widespread in nature, especially in standing-water lakes. Precise differentiation between these microbes in pure culture is possible only by serological tests (for example, agglutination).

Epidemiology. Cases of cholera now occur only in some countries of Asia and the Near East. Cholera was first brought into Europe in 1817; from then until 1925 mass incidence of the disease repeatedly recurred and during some periods developed into pandemics.

In the USSR cholera was *completely* eradicated in the middle of the 1920's.

The *Vibrio comma* gains entrance into the human organism with water or foodstuffs contaminated with it. The infection may also spread through hands contaminated with the faeces of a patient or carrier (for example, in caring for a patient, using a common toilet) and through flies.

Pathogenesis and pathologic anatomy. In the patient's organism the *Vibrio comma* particularly strongly affects the mucosa of the small intestine: the very rapid reproduction of the vibrios, their mass destruction and liberation of endotoxin damage the epithelium of the mucosa of the small intestine with the result that the epithelium desquamates and large amounts of water, protein and salts transudate through the intestinal wall. This gives rise to frequent diarrhoea, repeated vomiting, extreme dehydration of the organism, haemoconcentration and achlorhydria.

The salt deficiency, acidosis, tissue hypoxia and haemoconcentration disturb the haemodynamics and the renal function (to the point of anuria), and result in serious cardiovascular disorders and muscular cramps. The acute inflammatory changes in the gastric and intestinal mucosa cause severe gastroenteritis.

The general intoxication often also leads to respiratory disorders. The increased viscosity, amount of haemoglobin and number of erythrocytes denote haemoconcentration.

The corpse presents a characteristic appearance: sunken eyeballs and clearly outlined body muscles (due to dehydration and rigidity); all tissues are extremely dehydrated, the serous membranes are covered with a sticky lubricant, the serous membrane of the intestines and the mesentery have an expanded capillary network and are sometimes stained with bile (Fig. 25). The mucous coat of the small intestine is desquamated and superficially necrotized. Degenerative changes are found in the liver, spleen, kidneys, adrenals and the myocardium.

Clinical picture. The incubation period averages 2-3 days, but may be from 1 to 6 days. Three successive periods are distinguished in the development of the disease: (1) *choleraic diarrhoea*, (2) *choleraic gastroenteritis*, and (3) *atgid period*. It should be noted, however, that the disease must not necessarily go through all three periods and the disease may end with choleraic gastroenteritis or even choleraic diarrhoea.

The disease sets in acutely with *choleraic diarrhoea*. The patient develops weakness, nausea, and a frequent liquid yellowish-brown stool with a faecal odour, infrequently containing a very small amount of mucus. Within a few hours the patient begins to vomit repeatedly.

Choleraic diarrhoea is followed by *choleraic gastroenteritis*. The patient's stool becomes increasingly more frequent, loses its faecal character and resembles rice water—turbid, whitish liquid contain-

ing flakes of desquamated intestinal epithelium and an enormous number of cholera vibrios. The stool of some patients also contains mucus and sometimes blood. The patient vomits repeatedly, the vomitus, like the faeces, presenting an appearance of rice water.

Signs of extreme dehydration and general intoxication continue to increase. The heart sounds are dull, the blood pressure drops and the urinary output sharply decreases. Painful tonic spasms often appear. The tongue is coated with a dense white film and the abdomen is drawn in.

As the pathologic phenomena increase the patient enters *the algid period (algidus—cold)*. He is in a state of complete apathy, his temperature drops to 35-35.5°C, his extremities are cold, and dehydration is strongly pronounced. He is very weak, the integuments are pale, often with a cyanotic hue, the skin is covered with sweat and its folds hardly straighten out, the skin of the hands being particularly wrinkled (washerwomen's hands). The eyes are deeply sunken, the cheeks also appear sunken, all facial features are drawn, and the voice is very faint (*vox cholERICA*). The respiration is very rapid, urine is hardly discharged, and the abdomen is drawn in. The stool, although becoming less frequent than at the onset of the disease, is quite frequent nevertheless, and still looks like rice water; now and then it contains blood; the volume of the faeces decreases, compared with the first days of the disease, but the faeces continue to resemble rice water.

Vigorous treatment makes it possible to bring the patient out of this grave condition; however, during the algid period the patient may die; in particularly severe cases the patient may die at earlier stages exhibiting phenomena of collapse.

After abatement of the symptoms of the algid period some patients develop a dangerous complication—*choleraic typhoid*—which is characterized by a severe toxic affection of the brain (coma) or the kidneys. An important role in the onset of choleraic typhoid is played by secondary infection of the organism with an intestinal flora and development of acute sepsis.

There are *fulminant forms* of cholera characterized by clonic and tonic spasms and resulting in the patient's death already at the end of the first or the beginning of the second day. In cases of *cholera sicca* (dry cholera) the patient may die even before the appearance of vomiting and diarrhoea.

Atypical and effaced forms of the disease with only some of the symptoms and picture of diarrhoea and the absence of the characteristic stool, muscular spasms and marked dehydration of the organism occur much more frequently. These forms particularly frequently affect children. Repeated and careful bacteriological examination of the patient is absolutely necessary in all the foregoing forms of cholera.

Diagnosis. Identification of Asiatic cholera is a very important

function of the physician, since the occurrence of even a single case of the disease in the given area necessitates strict quarantine measures over a large territory. In establishing a diagnosis all epidemiological data (living in an endemic area and contact during the preceding week with patients and vibrio carriers) must be carefully considered.

In addition to carefully collected clinical and epidemiological data it is necessary to have a laboratory confirmation of the diagnosis, for which purpose 100-150 g of the patient's fresh faeces and vomitus are sent in sterilized, tightly closed and sealed jars to a bacteriological laboratory for examination. Before the answer is received from the laboratory strict anti-epidemic measures must be carried out, the patient must be isolated and the persons who had contact with the patient must be hospitalized separately.

To isolate cholera vibrios from the patient's organism, 1-2 ml of liquid faeces are inoculated in slightly alkalized 1 per cent peptone water to which a 0.5 per cent sodium chloride solution and a 0.01 per cent potassium nitrate solution (enrichment medium) are added beforehand. This nutrient medium is placed in a sterile tea glass covered with paper or in a sterile Erlenmeyer flask. A culture of the patient's faeces is additionally made in a similar nutrient medium poured into 3-4 test-tubes, which increases the probability of isolating cholera vibrios from the patient's stool. A culture of mucus clumps from the patient's fresh faeces is simultaneously made in alkaline agar in two Petri dishes. If the patient's faeces contain a large number of cholera vibrios, their growth in alkaline agar may be so rapid that a bacteriological confirmation of the diagnosis will be received within 18-24 hours without a preliminary culture of the faeces in 1 per cent peptone water. Cholera vibrios must develop in both the peptone water and the alkaline agar in a thermostat at 37°C.

Cholera vibrios grow on the surface of 1 per cent peptone water, their growth often being accompanied by formation of a thin film. During the first hours of their growth in this enrichment medium a film may not form, but the cholera vibrios multiply in the superficial layers of the liquid just the same.

Twice--6 and 12 hours after inoculation of the tested faeces in peptone water--a small amount of the liquid is taken from the surface with a platinum loop and is reinoculated in alkaline agar. The repeated reinoculations from the peptone water in agar increase the probability of isolating vibrios. After 18-24 hours of growth in agar at 37°C delicate, glasslike, transparent colonies are formed; these are taken off with a sterile platinum loop for reinoculation in slant agar to isolate a pure culture of cholera vibrios after 20 hours of growth in a thermostat at 37°C.

Smears are made on a slide glass from the pure culture thus prepared and are stained by Gram's method; besides, the motility of cholera vibrios is tested in a hanging drop. Whether or not the isolated vibrios are true cholera vibrios is ascertained by means of an agglutination test in test-tubes, for which purpose it is necessary to make use of a specific O-agglutination serum of a sufficiently high titre. The results of the agglutination test are noted twice--after letting the test-tubes stand in a thermostat at 37°C for 2 and 20 hours.

The following is an accelerated method of diagnosing cholera: 5 drops of the patient's liquid stool are placed in each of 4 test-tubes containing 10 ml of 1 per cent alkalized peptone water. Then anticholeraic serum is added in a 1 : 2000 dilution to the first test-tube and in a 1 : 1000 dilution to the second test-tube; a 0.1 per cent starch solution is added to the third test tube, while the fourth test tube serves as the control. If the patient's faeces contain cholera vibrios, the latter rapidly multiply and then agglutinate in the surface

layer of the peptone water, which is clearly visible to the eye, and the formed flakes slowly settle to the bottom of the test-tube.

Owing to the fermentative activity of the cholera vibrios the starch in the third test-tube quickly disintegrates, for which reason the liquid does not stain blue when several drops of Lugol's solution are added to this test-tube.

For purposes of a mass and rapid examination of people for cholera vibriocarrying Z. V. Yermolyeva's accelerated method is used. A small amount of faeces is taken directly from the rectum with a glass tube having bevelled edges and the corresponding end of the tube is immersed in a vial with a nutrient medium; in the absence of such tubes the faeces may be taken by means of a cotton tampon. Faeces from 10 tested persons are inoculated in the same vial.

The nutrient medium consists of 200 ml of 1 per cent peptone water+agglutinating choleraic O-serum diluted to half its titre; the vials are kept in a thermostat at 37°C for 5-6 hours, after which the formation of flakes which settle to the bottoms of the vials (agglutination of vibrios) becomes visible. Portions of the liquid are taken with a pipette from the bottom of the test-tube. Gram-stained smears on slide glass and a hanging drop are prepared, and various zooids and groups of agglutinated vibrios are discovered. The results of the test are known within 6 hours.

If cholera vibrios are discovered in any of the vials where the faeces of 10 persons have been tested, an individual culture of the faeces of each of these persons is immediately made according to the aforementioned method.

To prove that the vibrios isolated from the patient are true cholera vibrios, it is necessary, in addition to their aforesaid agglutination with a specific serum, to observe the phagolysis of the vibrios from the culture isolated from the patient. To do this, 0.2 ml of a specific choleraic bacteriophage is added to a 12-16-hour vibrio broth culture (in a weakly alkaline medium); after standing in the thermostat for 1-2 hours the culture becomes noticeably lucid or complete lysis is observed.

Differential diagnosis. The disease must be differentiated primarily from the most acute forms of salmonellal food poisoning (Table 1), acute dysentery, mushroom poisoning and poisoning with chemical substances.

Table 1

**Differential-Diagnostic Relations Between Acute
Salmonellal Gastroenteritis and Asiatic Cholera**

Acute Salmonellal Gastroenteritis	Asiatic Cholera
1. The disease begins with nausea and vomiting to which a frequent, liquid, watery stool is successively added	1. The initial stage of the disease is limited to a diarrhoeal symptom complex and only later, in the stage of choleraic gastroenteritis, is vomiting added to the diarrhoea. Nausea is not typical of cholera
2. A frequent and very liquid (watery) stool of a faecal character is retained at the height of development of the clinical picture; only now and then it presents the appearance of rice water	2. Characterized by a very frequent rice-water stool. Dehydration of the organism and loss of skin turgor are strongly pronounced
3. Muscular cramps are comparatively rarely observed and are limited only to the extremities	3. Many patients have clonic and tonic spasms

4. Abdominal pain often observed	4. No abdominal pain observed
5. Temperature curve at a rather high level; a saddleback curve is possible	5. Temperature normal or lowered
6. Abdomen usually inflated	6. Abdomen drawn in, boat-shaped
7. Tenesmus observed in many patients	7. Not typical
8. Urinary output scarcely disturbed	8. Urinary output sharply decreased to the point of anuria

Toxic dysentery is characterized by toxicosis, chills, tenesmus, spastic contraction and tenderness of the sigmoid colon on palpation, mucus and blood in the stool. In doubtful cases it is obligatory, taking all necessary precautions, to make repeated bacteriological tests of the stool.

The results of clinical examinations and bacteriological tests play a decisive part; in doubtful cases it is necessary to make many tests of the patient's faeces for cholera vibrios by means of cultures in 1 per cent peptone water.

Treatment. In cases of cholera the same diet is prescribed as in typhoid fever. To decrease dehydration and stimulate the cardiovascular functions, patients are given intravenous infusions of sterile physiologic solution heated to 40°C. The physiologic solution is administered in divided doses, a total of 3-6 litres per day (rate of administration—1 litre in 15 minutes). Instead of the foregoing method of administration it is recommended that up to 3-4 litres of the solution per day be infused intravenously by the drip method and single subcutaneous injections of 350 ml of 5 per cent glucose solution be additionally made into each thigh; for better absorption of the injected solution heat is applied to the sites of the injections.

It is necessary to stimulate the blood circulation by injections of ephedrine, cordiamine (nickethamine) and camphor. Literature contains recommendations for using such hardly soluble sulphonamides as sulgine (sulphanilylguanidine) [0.5 g six times per day for 4-6 days] with simultaneous administration of levomycetin (chloramphenicol) [0.5 g four times per day] or biomydin (chlortetracycline) [300,000 U four times per day]. Biomydin may be replaced by tetracycline in appropriate doses. Administration of biomydin together with sulgine is expedient. Satisfactory results are produced by treatment with terramycin (0.3 g six times per day for 3-4 days). Antibiotics do not guarantee recovery.

In addition to the treatment with antibiotics the patients should be prescribed bacteriophage—30-40 ml twice a day. In cases of collapse patients are given mesaton (meta-oxyphenyl methylaminoethanol hydrochloride), ephedrine, noradrenalin and massive drip intravenous and intramuscular infusions of physiologic solution.

General baths at a temperature of 35-35.5°C (for 8-10 minutes) with subsequent quick rubdowns with a Turkish towel are recommended; after the bath the patient must be put in a warm bed. The room must be kept warm and heat must be applied to the patient's feet. The patient must be given strong hot tea (in small portions because of repeated vomiting).

Prophylaxis. An important role in preventing cholera is played by sanitary control of the water supply, quarantine measures with respect to people arriving from areas where there are cases of cholera, revealment of carriers, and specific prophylaxis by means of subcutaneous injections of a cholera vaccine (killed cholera vibrios). The vaccinations are made to persons who are in real danger of contracting cholera (not later than 3 weeks before possible infection). The vaccinations against cholera may be combined with those against typhoid fever, paratyphoids, dysentery and tetanus.

Upon discovery of cholera cases in any area it is necessary, in addition to the strict quarantine and individual isolation of patients and vibrio carriers who have been in contact with them, to visit every house for the purpose of revealing cholera patients, who are immediately hospitalized, chlorinate the water, intensify the sanitary supervision of the water-supply sources and exterminate the flies in dwellings, as well as at their breeding sites.

Measures of phagoprophylaxis by means of a specific cholera bacteriophage are extensively carried out among the population in areas unfavourable as regards cholera; if necessary (mass incidence of the disease), these measures are supplemented by chemoprophylaxis with hiomycin and levomycetin.

All cholera patients and persons who have been in contact with them (distinguished according to the degree of contact) are subject to *very strict isolation*. Attempts must be made to isolate each patient *individually*. Rigid quarantine measures must be taken on the territory surrounding the given community or place where the patient has been discovered. Medical workers must immediately report each case of cholera to the higher public health bodies in keeping with the established procedure.

Patients with *any form of diarrhoea*, who were in the community where cholera cases were discovered, are subject to urgent and compulsory hospitalization.

The focus of the disease (apartment, hostel, place of work, etc.) must be thoroughly disinfected; the faeces and vomitus must be disinfected with a 10 per cent lime chloride solution; the attending personnel must wash their hands with a 0.5 per cent chloramine solution and then with hot water; the dishes used by the patient must be disinfected by boiling.

The ambulances used for transportation of cholera patients must have individual bedpans and rubber rings; after delivery of the patient to the hospital the ambulance and things used in the care



Fig. 23. Mucous membrane of the large intestine in amoebiasis.



of the patient must be disinfected. Thorough current and final disinfection with a 10 per cent clarified lime chloride solution must be carried out in the hospital.

The condition for the discharge of a convalescent is a clinical cure and threefold negative result of the patient's stool test made on the 6th, 8th and 10th days after disappearance of the clinical symptoms.

If a bacteriological test of the patient's faeces cannot be made, the patient may be discharged no sooner than the 14th day after disappearance of the clinical symptoms.

Persons who were in contact with a patient and vibrio carriers must be placed in separate isolators, for which purpose a special building must be adapted. The faeces of vibrio carriers are subjected to bacteriological tests every 5 days until a twofold negative result is obtained. During the following three months these persons must be examined three times for vibrio carrying and, if they turn out to be carriers, they must not be allowed to work in food-processing enterprises, dining-rooms, children's institutions, etc.

Persons who have been in contact with a cholera patient must be taken under observation and must be isolated for six days. During this period their faeces must be bacteriologically tested for cholera vibrios three times. All these persons must be given 20 ml of cholera bacteriophage every three days (on an empty stomach).

Upon appearance of even a single case of cholera in the isolator for persons who were in contact with cholera patients the quarantine period must be additionally prolonged to 6 days from the moment of individual isolation of the person who has fallen ill in the isolator. The faeces of all persons who were until then in the isolator must be tested for cholera vibrios twice more.

BOTKIN'S DISEASE (MORBUS BOTKINI)

(Epidemic Jaundice. Acute Infectious—Epidemic—Parenchymatous Hepatitis)

Botkin's disease is a general acute infectious disease caused by a filtrable virus (in cases of enteral infection); it occurs in the form of sporadic cases and outbreaks, runs a cyclic course and is accompanied by jaundice, affection of the liver and metabolic disorders.

Historical data. Botkin's disease undoubtedly occurred very early in human history, but the first authentic descriptions of epidemics of this disease appeared only in the 17th century. During the 19th century there were 112 epidemics and outbreaks of this disease. At times of war, national calamities and migrations of masses of people a greater incidence of jaundice, known as "catarrhal jaundice", is usually observed.

In 1883 the outstanding Russian clinician S. P. Botkin established by careful clinical observation that the so-called catarrhal jaundice was a general infectious disease and that it could spread epidemically.

Thus S. P. Botkin must be credited with establishing that catarrhal jaundice is a separate nosological entity and with proving that it is an infectious disease; that is why it is now called Botkin's disease.

Aetiology. The causative agent of Botkin's disease is a special type of filtrable virus (*Botkinia hominis*) which is found in the blood, bile and faeces of patients, particularly during the preicteric period and in the first 10-12 days of the icteric period. From the patient's organism the virus is eliminated in the faeces. No pure culture of the causative agent of Botkin's disease has as yet been obtained; its morphological features and other properties remain unclear.

The virus parasitizes mainly in epithelial cells, affecting primarily the parenchyma of the liver. It possesses considerable resistance to external influences (desiccation, freezing, and action of a number of disinfectants); for example, it takes 3-4 hours to inactivate it at 60°C.

It is assumed that the aetiology of Botkin's disease is identical with that of so-called *inoculation jaundice* (or syringe jaundice). The latter may develop in healthy people as a result of parenteral administration of even small amounts of blood or serum of a person, who is in the incubation or earliest icteric period of Botkin's disease during inoculations and intravenous, subcutaneous or intramuscular injections of drugs.

Epidemiology. A healthy person contracts the disease from a patient enterally by introducing the filtrable virus into his gastrointestinal tract with his own soiled hands contaminated with the patient's faeces, and with water, milk, and foodstuffs contaminated with the patient's excrements. The spread of the disease as an intestinal infection is also fostered by flies.

The patients are the most contagious during the preicteric period and in the first 10-12 days of the icteric period; however, they continue to be contagious also during the subsequent days of the disease.

Thus Botkin's disease is epidemiologically *an infectious intestinal disease*. This established, it is necessary to take appropriate anti-epidemic measures in many respects similar to those which are carried out in cases of dysentery or typhoid fever.

Some authors hold that the disease is transmitted by means of droplets containing the causative agent, i.e., that it is an airborne or droplet infection.

Although Botkin's disease may occur as sporadic cases all year round, the maximum disease incidence is observed in September and October.

In addition to sporadic cases there may be epidemic outbreaks and even considerable epidemics, as often happened in the past.

The only source of infection is a patient who is contagious mainly during the preicteric period and in the first 10-12 days of the icteric period. In a number of cases a careful epidemiological investigation helps to find this source. All patients are subject to compul-

sory hospitalization. In the patient's apartment or hostel in which he lived a moist disinfection is performed (according to the same rules as in cases of other intestinal infections) after his hospitalization.

There are atypical, including *anicteric* and effaced forms of Botkin's disease, which, if unidentified, constitute a serious epidemiological factor.

Pathogenesis and pathologic anatomy. Upon entering the gastrointestinal tract the causative agent of Botkin's disease produces inflammatory changes in the gastrointestinal mucosa and through the walls of the blood capillaries passes into the blood stream thereby bringing about the general symptoms of the infection, the temperature reaction in the first place.

In the epithelial cells of the liver the virus multiplies and produces a number of anatomic changes in the hepatic parenchyma. The development of the disease disturbs the participation of the liver in carbohydrate, protein, water-salt and vitamin metabolism. A large amount of bile pigments and bile acids enters the general blood circulation and gives rise to such important symptoms of Botkin's disease as icteric discoloration of the skin, mucous membranes and sclerae, and itching of the skin.

Today Botkin's disease rarely ends lethally, but death is possible if the disease becomes complicated with *acute yellow atrophy of the liver*.

Acute yellow atrophy of the liver is characterized by severe degenerative and necrotic processes, to the point of impairing the normal hepatic architecture. The stroma of the liver assumes a reticular appearance, and many fatty and protein grains are discovered in the hepatic and the Kupffer's cells.

The enlargement of the liver is connected with phenomena of congestion and proliferation; in cases of atrophy the liver considerably contracts.

Clinical picture. The incubation period of Botkin's disease is close to 50 days and in cases of syringe (inoculation) jaundice much longer—up to 200 days.

Under usual conditions of enteral infection the disease begins with a preicteric period which lasts from 2 to 10 days.

The preicteric period is characterized by a disturbance in the patient's general condition (jadedness, rapid fatigability, headache, considerable nervous excitement). Many patients (50-75 per cent) exhibit dyspeptic phenomena manifested in a loss of appetite, pressure in the pit of the stomach, nausea, repeated vomiting and heartburn. An unstable stool with alternating constipation and diarrhoea is often observed.

The manifestations of the preicteric period include *arthralgias* which occur in about 25-30 per cent of all cases. There are pains in the shoulder, hip and knee joints; the joints do not change in size and the skin over them retains its normal colour.

One of the early manifestations of the disease is a change in the colour of the urine which becomes a saturated brown (beer colour); simultaneously, or 1-2 days later, the liver gradually begins to enlarge; a heaviness and a dull pain are felt in the right hypochondrium.

This period is followed by the *icteric period* which determines the peculiarities of the disease.

At first the icteric discoloration is noticeable on the sclerae and on the hard palate; then jaundice can easily be seen on all of the skin and the visible mucosa. In the beginning the skin is light-yellow (canary-coloured), then the colouring gradually grows deeper and reaches its maximum between the 12th and 14th days of the icteric period.

Between the 15th and 20th days of the disease the skin becomes orange-coloured. The intensity of the colouring diminishes just as gradually. The skin must be examined only in daylight.

Discoloration of the stool becomes noticeable between the 3rd and 11th days, the stool turning greyish-white ("clayey"); this discoloration lasts 10-15 days and is due to the fact that bile temporarily fails to enter the intestine because of the considerable swelling of the liver and compression of bile capillaries and ducts.

Usually the temperature does not rise very high and the febrile reaction lasts only 5-8 days.

With the intensification of the icteric discoloration of the skin many patients develop pruritus (itching) owing to irritation of the sensory nerve endings in the skin by bile acids. The itching may gradually become so tormenting as to disturb sleep and the patient's general state.

Sometimes patients exhibit haemorrhagic phenomena (bleeding from the nose and gums, and abundant menses) which are due to the increased permeability of the blood capillaries under the action of bile acids, a decrease in the thrombocytes of the blood and diminished production of prothrombin by the liver.

Many patients exhibit dyspeptic phenomena: a feeling of heaviness in the epigastrium, nausea, often repeated vomiting, eructation, heartburn and an unstable stool. The disease is accompanied by disturbances in the motor and evacuant functions of the stomach; moreover, the acidity of gastric juice and the amount of free hydrochloric acid in it considerably decrease.

The enlargement of the liver may be observed already during the preicteric period; during the following 10-15 days of the disease the liver continues to enlarge, becomes painful on palpation (because of the distention of Glisson's capsule) and somewhat indurated. As the patient recovers the liver grows smaller, but owing to the development of regenerative processes it may long continue to be quite indurated. The liver may enlarge to various extents. For the purpose of controlling the size of this organ, it is measured

(in cm) vertically along the right midclavicular, axillary and median lines.

The lower border of the liver is usually roundish and somewhat painful to touch.

The spleen enlarges in about 45-65 per cent of the cases; its lower border protrudes 1-2 cm from under the costal arch and is sensitive on palpation.

In cases of acute yellow atrophy of the liver hepatic insufficiency is accompanied by severe neuropsychic disturbances, to the point of coma.

At the height of development of the icteric period the blood picture is characterized by leucopenia (with about 4,000-4,500 leucocytes per 1 cu mm); a relative lymphocytosis (up to 60-65 per cent lymphocytes) is observed at the same time. During the period of convalescence some patients sometimes exhibit monocytosis. The ESR is somewhat below normal.

Botkin's disease is characterized by a general disturbance in metabolism, pigment metabolism in the first place. Normally bilirubin is formed in the Kupffer's reticuloendothelial cells of the liver. The disease impairs the ability of the hepatic cells to excrete bilirubin which is normally excreted through the bile ducts into the intestine; large amounts of this pigment therefore enter the blood and produce jaundice. The amount of bilirubin in the blood considerably increases (instead of the normal 0.6-0.8 mg%, as determined by van den Bergh's method the patients affected with Botkin's disease may have 6-10-20 mg% and in some cases even 20-30 mg% bilirubin).

In Botkin's disease the qualitative reaction to bilirubin is usually *direct* (to determine the bilirubin in these cases no preliminary sedimentation of the blood serum proteins is required), which indicates damage to the hepatic cells since they usually remove the excess bilirubin from the blood.

As a rule, the increased content of bilirubin in the blood is paralleled by an increased elimination of bile pigments in the urine. The amount of bile pigments eliminated in the faeces decreases in the very beginning of the disease and by the time the stool is temporarily discoloured stercobilin (i.e., bilirubin oxidized in the intestine) is either entirely absent or is eliminated in the faeces in extremely small amounts.

Owing to the disturbances in pigment metabolism marked urobilinuria is found during the first days of the disease, but with the development of the icteric period it diminishes, to the point of complete disappearance of urobilin, during the period of temporary discoloration of the stool when hardly any bile enters the intestine.

As the patient recovers, the amount of bilirubin in the blood decreases to normal, and the urobilinuria, the patient had there-

tofore, disappears; the normal colour of the stool and the elimination of stercobilin in the faeces are restored somewhat earlier.

The disorders of carbohydrate metabolism and the disturbances in the glycogenetic function of the liver are very clearly revealed by functional tests, including, for example, the sugar load test (the patient ingests 100 g of sugar on an empty stomach, after which the content of sugar in the patient's blood is determined every 30 minutes for 2-2.5 hours). In Botkin's disease the sugar curve is usually disturbed: it rises gradually and returns to normal very slowly.

The functional state of the liver may be revealed by a number of sedimentation and colloid tests, for example, the Takata-Ara fuchsin and mercuric chloride test, thymol, thymol-veronal, and Weltmann's tests, and determination of aldolase and transaminases I and II.

Botkin's disease is characterized by disturbances in lipid metabolism, a decrease in the amount of cholesterol in the blood being one of the very frequent biochemical signs of the disease.

From the third or fourth week of the disease the patient's condition begins to improve, and the pathologic symptoms gradually disappear. The skin and visible mucosa pale, and following the disappearance of the jaundice the liver contracts, the amount of bilirubin in the blood diminishes, the appetite is restored, and itching ceases. However, the patient must stay in bed until all the functions of the organism are sufficiently restored, which may be judged by the disappearance of the clinical symptoms and the results of repeated functional tests. The patients are not allowed to smoke, eat seasoned food and consume spices and alcohol for the duration of the disease and for two months after discharge from the hospital.

Only when it becomes clear that the patient has quite recovered and, if possible, after blood tests for bilirubin and various functional tests is the patient discharged from the hospital. It should be remembered that Botkin's disease sometimes runs a *protracted* and even a *chronic* course. This may be fostered by violations of the regimen and premature discharge from the hospital.

In the *protracted* form of the disease the icteric discoloration of the skin is retained, the bilirubin reaction of the blood remains direct and accelerated, the amount of bilirubin is much greater than normal, and the liver is enlarged and painful for 2-3 months and even longer. Other manifestations of the disease are also possible.

Such cases require thorough medical observation and particularly good care. After discharge from the hospital many convalescents should be recommended health-resort treatment.

Careful differential diagnosis is required in cases of obstructive (mechanical) jaundice caused by compression of the bile ducts

(this condition is most commonly caused by cancer of the head of the pancreas).

In *chronic* forms of Botkin's disease periods of aggravation alternate with remissions; these forms may last 2-3 years, but they are observed infrequently.

Both the protracted and chronic forms of the disease may lead to development of *cirrhosis* of the liver.

From two to four weeks after apparent recovery some patients may suffer relapses which resemble the primary attack of the disease.

The disease confers unstable immunity; cases of repeated attacks of the disease, rather infrequent, to be sure, have been observed.

The usual course of Botkin's disease may be disturbed by various complications (see below).

Prognosis. Botkin's disease usually ends in complete recovery, but in a small number of cases it assumes protracted and even chronic forms.

The disease is the most frequent cause of cirrhosis of the liver; the possibility of development of cirrhosis is attested by a protracted enlargement of the liver, its considerable induration and stable disturbances in pigment metabolism (bilirubinaemia); elevated, dark-red, wartlike spots (telangiectases) appear on the skin.

In cases where acute yellow atrophy of the liver develops the prognosis becomes very serious.

Complications. *Acute yellow atrophy of the liver* is the gravest complication of Botkin's disease. Most commonly it develops when the disease runs a severe course, during the second half of the icteric period, but there are cases in which acute atrophy is observed already on the sixth or seventh day of the disease. Progressive adynamia, complete absence of appetite, considerable sleepiness during the daytime with insomnia at night, and often intractable vomiting, rise in temperature, and leucocytosis are danger signals of incipient atrophy of the liver.

The patient's respiration is accelerated and a petechial eruption breaks out on the skin. It is characteristic that the liver contracts, is indurated and painful; it contracts rapidly—in the course of 2-3 days.

The initial stages of atrophy of the liver are marked by general neuropsychic excitement which in some cases goes to the extreme (delirium, aggressive actions) and is followed by *hepatic coma*. In some cases hepatic coma is not preceded by the stage of excitement.

In the initial stages of coma the patients are in a dejected mood and may have hallucinations. Bleeding from the nose, gums and intestines is often observed; the skin shows petechiae. The liver is contracted and painful. The blood exhibits leucocytosis and a high bilirubin content. The respiration is accelerated, the patient's

breath has a peculiar "hepatic" odour, the pulse is rapid, the pupils are dilated, the abdominal and tendon reflexes are weak or even absent. Meningeal phenomena and spasmodic twitchings of various muscles are clearly marked. Epileptiform seizures, involuntary urination and defaecation are possible.

With the onset of coma the prognosis becomes very serious, but in a number of cases timely and vigorous complex therapy (massive infusions of glucose and physiologic solution, injections of cortisone or administration of prednisone) makes it possible to bring the patient out of the extremely grave condition. A subacute course of the atrophy is possible.

Sometimes Botkin's disease is accompanied by formation of ascites—*oedematous-ascitic form*.

Diagnosis. In establishing a diagnosis of Botkin's disease it is necessary to take into consideration the epidemiological data, the anamnesis, clinical picture and results of the biochemical tests.

Botkin's disease must be *differentiated* primarily from ictero-haemorrhagic leptospirosis (Weil-Vasilyev's disease) and ictoric forms of anicteric leptospirosis; in these cases it is necessary to take into account the corresponding clinical and laboratory data typical of leptospirosis (see "Weil-Vasilyev's Disease and Anicteric Leptospirosis").

In patients past 40-45 years of age and, especially, in elderly persons exhibiting jaundice it is necessary to differentiate the disease from *obstructive* (mechanical) jaundice caused by neoplasms in the abdominal cavity (most frequently—cancer of the head of the pancreas or cancer of the ampulla of Vater).

The main differences between Botkin's disease and obstructive jaundice are shown in Table 2.

Obstructive jaundice exhibits stable bilirubinaemia which tends to increase, the skin is orange-coloured or of a greenish-earthy hue, the stool is discoloured for a long time, the faeces contain either very little stercobilin or none at all. True, in cases of cancer of the ampulla of Vater the colour of the stool may temporarily be restored because of the disintegration of the tumour, but the faeces then contain concealed blood.

During the first 6 weeks following the appearance of obstructive jaundice the functional liver tests are little disturbed and the cholesterol is high. Larger amounts of ether-soluble bilirubin (more than 2 mg%) are often established from the end of the first month of the disease. In some patients it is possible to palpate a dilated gallbladder (Courvoisier's symptom). Cancer of the head of the pancreas in the terminal period is often accompanied by a disturbance in the balance of the diastase of the blood and urine; the amount of diastase in the urine is considerably increased.

In a number of cases where Botkin's disease is suspected it is necessary to establish a differential diagnosis with hepatitides of

toxic and septic origin, which are connected with acute leucosis, sepsis of various aetiology, including anaerobic infection, thyrotoxicosis, occupational intoxication, acute haematogenous tuberculosis and mononucleosis. Haemolytic jaundice connected with the development of sepsis and hepatocholecystitides of various aetiology must not be overlooked.

As a primary disease *the haemolytic disease* most frequently manifests itself in young persons and is characterized by moderate jaundice, anaemia and decreased osmotic resistance of erythrocytes.

Treatment. In Botkin's disease hospitalization is absolutely obligatory; all patients must stay in bed until disappearance of the clinical symptoms and normalization of the most important hepatic functions.

The patient is prescribed a dairy and vegetable diet with a limited amount of fats (the patient may consume up to 40 g of butter per day; it is necessary to exclude mutton fat, lard and other refractory fats). The food must be ingested in semi-liquid form 4-5 times per day. The total caloric value must be about 3,000-3,200 Cal per day.

All manner of seasoned dishes, fried meat and fish, sauerkraut, pickles and canned foods must be excluded. Acidophilous and other kinds of soured milk and fresh curds are indicated.

Patients should be given up to 400 g of curds per day. They must consume sufficiently large amounts of carbohydrates, for which purpose they are prescribed sweet dishes, large quantities of sugar, preserves, jam, sweet tea and honey; the patient's usual diet must be supplemented with sweet fruit, and vegetable, fruit and berry juices. The patients must be given only boiled meat and fresh boiled fish.

An important role in the treatment of the patients is played by improved glycogenesis in the liver; for this purpose intravenous infusions of 1.5-2 litres of a 5 per cent glucose solution are made by the drip method in the course of 24 hours, or the same amounts of the same solution are infused (preferably by the drip method) subcutaneously and intramuscularly.

It is necessary to administer ascorbic acid per os and intravenously in a dose of 0.6-0.8 g per day. Very limited application is found for methionine (1 g 4 times per day for adults); the latter may eliminate fatty infiltration of the liver, but in the acute form of Botkin's disease the infiltration is not pronounced, and the use of methionine is therefore inadequately substantiated theoretically and is unconfirmed by therapeutic practice.

The use of lipocaic and vitamin B₁₂ has also proved inexpedient. Many clinicians recommend prescription of alkaline mineral waters and 1 per cent magnesium sulphate (Magnesium sulfuricum) 1 litre of which is to be drunk per day. Abundant drinking is generally indicated for these patients. The patients must keep to the prescribed diet for 8-9 months after their discharge from the hospital.

From the moment acute or subacute atrophy of the liver has developed the patient must be particularly vigorously administered glucose. Daily intravenous infusions of 3 litres of a 5 per cent glucose solution by the drip method are recommended. In addition, it is necessary to give the patient a daily subcutaneous infusion of 1 litre of a 5 per cent glucose solution. Administration of cortisone (100-150 mg twice a day), prednisone, prednisolone and analogous hormonal preparations is indicated during the very early stages of atrophy of the liver; they are also administered in severe cases.

During the treatment with these preparations it is necessary to control the content of potassium and sugar in the blood and to test the urine for sugar; if the blood contains too little potassium (17.5-22.5 mg% is normal), the patient must be given potassium chloride in a dose of 1 g 4 times per day and must drink it down with half a glassful of warm water. Consumption of sodium chloride is limited to 2 g per day.

The patient is given hot sweet tea; the personnel of the department must see to it that the patient should drink a good deal. Moreover, a 5 per cent glucose solution must be administered per rectum by means of a nutritive enema. To prevent coma, administration of choline chloride (5 ml 4 times per day for several days) per os is recommended; this preparation should be administered even during coma since it sometimes produces a favourable effect, although it does not decide the success of the therapy.

In cases where hepatic coma has already developed the cardiovascular and respiratory functions have to be supported by injections of cordiamine (nickethamine), ephedrine, lobeline and cytitone, and subcutaneous administration of physiologic solution. In protracted cases the patients should be given prednisone (see supplement "Prescription").

With the modern methods of treatment mortality from Botkin's disease is no more than 0.1-0.2 per cent, but in cases of atrophy of the liver the prognosis is always serious.

Patients who have had an attack of Botkin's disease may be discharged from the hospital only after disappearance of the clinical symptoms (control of the level of bilirubin in the blood and indices of the functional tests is desirable), but not until 25 days from the beginning of the icteric period (period of communicability). After the discharge the patients should be given 10-day leave with obligatory report to the dispensary and subsequent observation for a period of 1 year. Health-resort treatment is recommended in severe cases after abatement of the clinical symptoms.

Prevention. Extensive health education of the population with emphasis on observance of the rules of personal hygiene (especially the necessity of washing hands before meals) is required. Efficient water supply and sewerage in all populated areas, and control of flies prevent the spread of Botkin's disease.

Differential-Diagnosis Signs of Botkin's Disease and Mechanical (Obstructive) Jaundice

Symptoms	Botkin's Disease (Epidemic Hepatitis)	Mechanical Jaundice
Prodromal (preicteric) stage	+	—
Pains in the joints	+	—
Girdle pains	—	+ (Cancer of the pancreas)
Elevated temperature	+	In some cases, rarely elevated
Enlarged spleen	+	—
Colour of skin	Light-yellow (canary or lemon) with subsequent change to darker (orange) hues	Greenish-earthy shade of jaundice; appears without preceding prodromal phenomena

(Continued)

Symptoms	Folk's Disease (Epidemic Hepatitis)	Mechanical Jaundice
Colour of faeces	Temporary discoloration	Stable discoloration (in disintegration of cancer of the ampulla of Vater the colour may vary)
Courvoisier's symptom	—	+
Haemogram	Leucopenia, relative lymphocytosis, neutropenia, low ESR	Tendency to moderate leucocytosis or normocytosis; high ESR
Reaction to bilirubin in the blood	Direct, rapid	Direct
Amount of bilirubin in the blood	Increased (in some patients to 30-35 mg%, according to van den Bergh)	Increased, but bilirubinaemia is moderate
Ether-soluble bilirubin in the blood plasma	Positive, but in small amounts in a small number of cases	Often positive with increased content in the blood
Bilirubin in the urine	+	++
Urobilinogen	++	— or ±

Stercobilin	+	temporary absence in discoloured faeces possible	— (Stable discoloration: in cancer of the ampulla of Vater the colour of the stool is temporarily restored and then is +)
Blood in the faeces		—	+ (in cancer of the ampulla of Vater)
Functional liver tests (thymol, mercuric chloride, etc).		Disturbed	Undisturbed during the first 1.5 months
Cholesterol in the blood plasma		Lowered	Normal or increased
Blood diastase		Undisturbed	Diastase balance disturbed in the terminal stage of the disease
Urine diastase		Undisturbed	
Serum phosphatase		Normal or slightly increased	Greatly increased
Aldolase activity		Increased	Normal
Blood plasma prothrombin after vicissol test		Remaining low or slightly increases	Increased
Abdominal pains		Not observed	Very inconstant sign, possible in insinuation of the peritoneum and in some cases of cancer of the pancreas

Early revealment of patients with compulsory hospitalization and thorough disinfection in the focus and at the patient's bedside, observing the same rules as in typhoid fever, are absolutely obligatory.

The patients' excrements containing the virus are rendered harmless by putting into the chamberpot or bedpan an amount of lime chloride equal to that of the excrements (the contents of the pot or pan must not be dumped into the sewerage for at least 3 hours).

In severe cases the patients must be given individual bedpans. All patients must have individual dishes, knives and forks which must be carefully sterilized by boiling each time they are used by a patient.

To prevent Botkin's disease, intramuscular administration of up to 15 ml of gamma-globulin was formerly recommended to persons who had been in close contact with patients; according to observations, this somewhat reduces the incidence of the disease or renders its clinical course milder; however, the effectiveness of gamma-globulin still requires careful study.

To prevent syringe (inoculation) jaundice, the syringes and needles must be thoroughly sterilized by boiling for 30 minutes before each infusion in all hospitals, polyclinics, etc., wherever these infusions are made. Persons affected with Botkin's disease and confined to special hospitals are assigned individual syringes and needles which are used only for these persons.

HELMINTHIASES

The term *helminthiases* refers to a group of human diseases resulting from infestation of the organism by parasitic worms (helminths) which have different biological properties. The role of helminths in the origin of human disease has long attracted the attention of physicians.

In the middle of last century the role of parasitic worms in human pathology was studied in greater detail. In 1884 S.P. Botkin pointed out the connections between the development of anaemia and the presence of helminths in the intestines, the action of the helminths manifesting itself through direct intoxication of the organism and neuroreflexly from the numerous receptors in the intestines.

The scientific studies of the aetiology, diagnosis, clinical aspects and therapy of helminthiases have resulted in serious achievements in the control of these diseases; special mention must be made of the works of Soviet investigators, particularly those of K. I. Skryabin, E. N. Pavlovsky, N. N. Plotnikov, V. P. Podyapolskaya and F. F. Talyzin. Helminthology has developed into a very important branch of biology and medicine.

The development of scientific knowledge in the field of helmin-

thology has opened up extensive opportunities for the control of helminthiases and has made it possible to prevent these diseases.

It is now entirely possible to eradicate a number of helminthiases on the territory of the USSR.

A brilliant example of eradication of foci of helminthiasis in the USSR is the successful control of dracunculosis which, until the 1920's, was extremely widespread among the people of Central Asia. The eradication of dracunculosis, achieved with the active participation of the prominent Soviet scientist L. M. Isayev, shows what fruitful results can be produced by combining theory and practice. The eradication of dracunculosis was accomplished by keeping careful records of all patients, their surgical treatment, and sanitation of the water reservoirs containing the species of cyclops which are the intermediate hosts to the nematode parasite *Dracunculus medinensis*.

At the same time it should be remembered that helminthiases are still considerably widespread among various sections of the population, especially children.

The overwhelming majority of the species of helminths parasitize in the human intestines. The group of parasitic worms which play the most important role in human pathology includes the *nematodes* (roundworms, thread-worms, trichinas and whipworms) which cause diseases known as *nematodoses* and a number of worms which belong to the class of *Cestoda* (broad tapeworm, dwarf, beef and pork tapeworms) which cause *cestodiasis*.

Outside the intestines some of the helminths can parasitize in various human tissues and organs (mainly only during certain phases of their cyclic development); for example, during its larval stage the *Trichinella* parasitizes in the muscles. Some helminths can also parasitize in the organism of various animals; that is why, for example, man may contract trichinosis by consuming the flesh of hogs infested with trichinas.

Numerous clinical observations have shown that, in addition to their own pathogenic role in healthy human beings, helminths may considerably aggravate the course of a number of acute infectious diseases, especially diseases affecting the intestines (dysentery, typhoid fever).

The following are the most important forms of helminthiases.

Nematodoses

Ascariases

The infestation of man by ascarids (*Ascaris lumbricoides*) which parasitize in the small intestine results in a morbid condition known as *ascariasis*. Ascarids are slightly spindle-shaped roundworms. The females reach a length of 25-40 cm, the males - 15-22 cm.

Both males and females can parasitize in the human intestines. If only females are present, the patient's faeces contain ovally elongated, pear-shaped or triquetrous unfertilized eggs covered with a protein membrane and containing yolk cells.

In the human intestines in the presence of a male ascarid a female ascarid can lay 200,000-220,000 round fertilized eggs. Ascarid eggs are noted for their considerable resistance to various harmful influences; they mature in the soil, if the latter is sufficiently aerated and has a certain temperature (24-30°C) and moisture.

Only the mature eggs of ascarids introduced into the mouth with dirty hands, raw and unwashed vegetables, fruit and berries contaminated with earth, and, in a number of cases, water containing the eggs of these helminths may cause infestation of man by ascarids.

After gaining entrance into the human intestines the eggs of ascarids shed their membrane and give rise to larvae which penetrate through the intestinal wall into the blood stream—branches of the portal vein. With the blood flow they enter the liver and the inferior vena cava, thence the right heart and then through the pulmonary artery gain entrance into the lungs. Passing through the walls of the pulmonary capillaries the larvae enter the alveoli, bronchioles, bronchi and trachea and then the oral cavity (Fig. 26).

In the oral cavity they mix with saliva and are swallowed again, regaining entrance into the small intestine.

In the intestine of an infested person the larvae of the ascarids continue to grow and develop into sexually mature males and females (Fig. 27). The complete cycle of this development takes ten weeks; the ascarids parasitize in the human organism for about 1 year.

Not infrequently many ascarids parasitize in the human intestine; this leads to marked intoxication of the organism and sometimes may cause mechanical obstruction of the intestine (ileus) by a cluster of ascarids; moreover, the patient's organism is sensitized by the waste products of the ascarids.

Clinical picture. The clinical symptoms of the early migration stage of development of the ascarids affecting the respiratory system are elevated temperature, coughing with a discharge of sputum which contains eosinophils, presence of pulmonary infiltrates or pneumonic foci in the lungs, and eosinophilia in the peripheral blood, which indicate an allergic reorganization of the organism. It must be admitted that during this early migration stage it is extremely difficult to diagnose ascariasis.

Intestinal ascariasis may run a concealed (latent) course, but may also show a marked clinical picture.

Most commonly, however, there are sufficiently clear clinical signs of ascariasis.

The symptoms of ascariasis are a diminished appetite, dizziness,

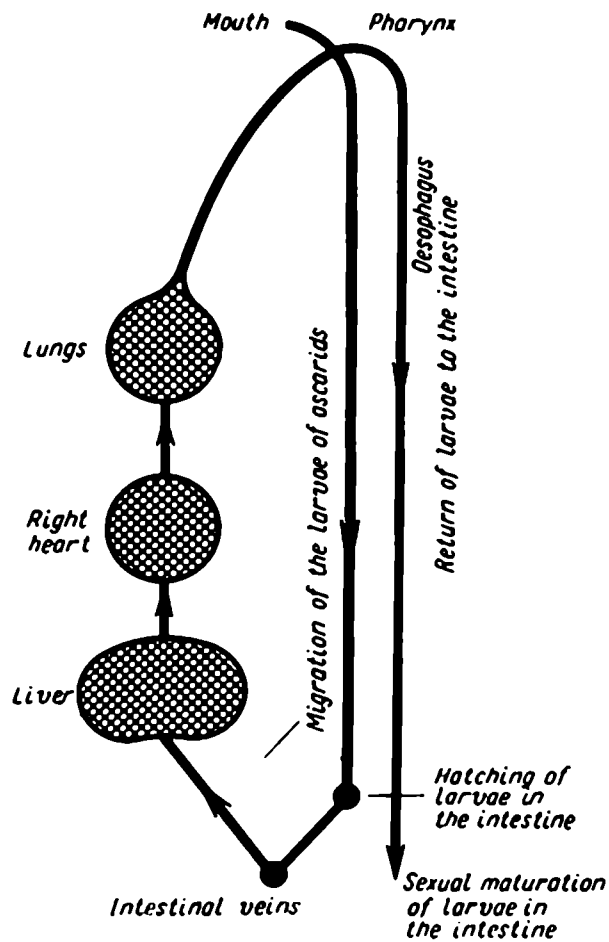


Fig. 26. Diagram showing migration of larvae of ascarids (from L. N. Pavlovsky)

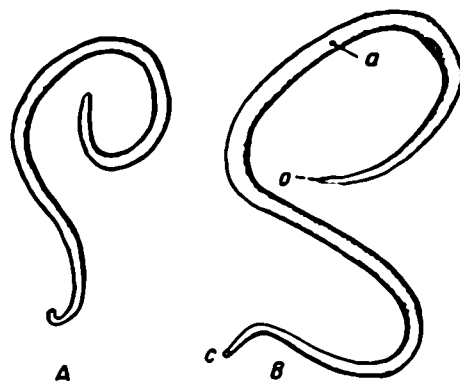


Fig. 27. Ascarids
A—male, B—female
a—sexual orifice; b—oral end; c—tail end

nausea, and a feeling of heaviness and pressure in the pancreatic region; ascariasis is often characterized by salivation, teeth-grinding at night, abdominal pain and considerable flatus. Children affected with ascariasis exhibit absent-mindedness, a dejected mood, disturbed sleep, nocturnal hallucinations and persistent headache.

Objective examination reveals but inappreciable signs of pathology: slight soreness in the epigastric and right iliac regions on palpation of the abdomen, moderate eosinophilia in the blood during the early stage of the disease, and, for the most part, low acidity of the gastric juice.

Ascariasis may be *complicated* (most commonly in children) by functional or mechanical (by a cluster of ascarids) ileus with a possible development of peritonitis and in some cases ascariasis of the liver and bile ducts.

Diagnosis. Ascariasis can be diagnosed by the character and localization of the abdominal pains with due consideration (during early stages of the disease) of eosinophilia in the blood and necessarily repeated helminthoscopic examination by the methods of Fülleborn and Kallantaryan, and by means of a native (unstained) smear.

Treatment. Chemical (santonin, sancaphene and piperazine) and physical agents are used in the treatment of ascariasis. Physical dehelminthization is carried out by introduction of oxygen into the intestine through a sound; since ascarids are anaerobic parasites they are quite rapidly destroyed.

Santonin is the active principle of *santonica* seed. During the treatment with santonin the patient is prescribed a diet of readily assimilable, mainly dairy and vegetable foods with a limited amount of fats. For adults the average therapeutic dose is 0.1 g. On the eve of the treatment the patient is given a saline laxative. The course of treatment is 2 days.

Santonin is taken on *an empty stomach* in a dose of 3 powders (pills) of 0.1 g each at 1-hour intervals; after taking the third powder (pill) the patient is given 25 g of magnesium sulphate or of another saline laxative; one hour later the patient may be given a light breakfast. On the second day the treatment is repeated. In treatment with santonin it is necessary to exercise caution (because the preparation is toxic) and to consider the contraindications, namely, diseases of the liver and kidneys, gastrointestinal diseases, and acute infections.

Clinical observations have shown the superiority of the Soviet preparation sancaphene dispensed in the form of pills containing 0.016 g of santonin, 0.0065 g of calomel and 0.016 g of phenolphthalein; this preparation simultaneously acts as a laxative. The course of treatment is 2 days.

On the eve of the treatment the patient is given a saline laxative (30 g of magnesium sulphate for adults). The following morning

the patient takes on an empty stomach 5 pills of sancaphene one after another, and 30 minutes later 5 more pills; then the patient is given a saline laxative. Two hours after taking the second dose of the preparation the patient is given a light breakfast.

The effectiveness of dehelminthization is judged by the elimination of dead ascarids in the faeces and the disappearance of the eggs of ascarids from the stool during repeated helminthoscopic examinations.

More physiologic, absolutely harmless and, what is more, sufficiently effective is *oxygen therapy* which results in complete dehelminthization in 80-85 per cent of the cases.

According to the modified method of N. P. Kravets (1951), 1,200-1,500 ml of oxygen is introduced under a certain pressure through a duodenal sound from a Richardson double rubber balloon into the patient's duodenum (on an empty stomach). On an average of 2-3 days after the oxygen therapy dead ascarids are eliminated in the patient's faeces. Usually two sessions of oxygen therapy with a 2-3-day interval are required.

Heptylresorcinol and piperazine may also be used for the treatment of ascariasis.

The former is dispensed in pills of 0.1 g each, covered with a special coating which prevents their disintegration in the stomach. The daily dose of heptylresorcinol for adults is 1.2-1.5 g; the course of treatment is one day. On the eve of the treatment the patient is given a saline laxative; the following morning the patient takes (on an empty stomach) the entire dose of heptylresorcinol, i.e., 12-15 pills 0.1 g each, in the course of 30-40 minutes; owing to the irritating action of the preparation on the oral mucosa the pills must not be chewed. Heptylresorcinol is contraindicated in cases of gastric and duodenal ulcers. Acid and salt food is prohibited.

The most effective of all dehelminthizing preparations so far proposed is *piperazine* which is dispensed in the form of piperazine adipate, piperazine sulphate, piperazine phosphate and piperazine citrate, all of them producing similar therapeutic effects. The preparation is dispensed in pills of 0.25 and 0.5 g and must be stored in a dark place in a tightly closed vessel.

Piperazine preparations are administered per os in equal doses and according to the same scheme.

In ascariasis the preparations are administered in doses of 1 g 3 times per day 0.5-1 hour after meals for two days in succession.

Doses for children:

1 year old	—0.2 g 2 times a day
2-3 years old	—0.3 g 2 " " "
4-6 " "	—0.5 g 2 " " "
7-9 " "	—0.5 g 3 " " "
10-14 " "	—1 g 2 " " "
15 years and older	—1 g 3 " " "

After the end of the treatment, in cases of constipation the patients are given a laxative. The diet before and during treatment is as usual.

Enterobiasis

The disease is caused by threadworms (*Enterobius vermicularis*), small round white worms. The female worms are about 1 cm long, the males—2-5 mm. The rear end of the female body is pointed, while that of the male is spirally twisted. Threadworms lodge in the inferior portion of the small intestine, but may also parasitize in the large intestine, crawling out through the anus.

Children are affected with enterobiasis particularly frequently. The infestation occurs when eggs (with motile larvae) are introduced into the mouth with contaminated hands as a result of contact with enterobiasis patients and somewhat less frequently by consumption of unwashed fruit and vegetables contaminated with the soil.

From the mouth of the infested person the eggs of threadworms enter the stomach and intestines. In the small intestine of man the eggs mature. The young parasites firmly attach themselves by suction to the intestinal wall; when the female worms reach sexual maturity they crawl out of the intestine and lay a large number of eggs around the anus and in the perianal folds. After laying the eggs the females die. Threadworms live for about 1 month.

Threadworms crawl out of the intestine mainly at night, hence the intense itching which so discomforts the patients. Owing to this the patients, especially children, scratch the skin in the anal region and thereby contaminate the hyponychial spaces and the tips of the fingers. This makes possible reinfestation through the mouth, which is particularly frequently noted in persons failing to observe the rules of personal hygiene (washing the hands before meals, trimming the nails).

The early *clinical manifestations* of the disease include intense itching in the anal region and the perineum, and in women, additionally, in the region of the external genitalia. At first the itching appears only at night, but subsequently may discomfort the patients all day long.

Enterobiasis in children is characterized by general nervous excitability and irritability. The children begin to lose appetite, become cranky, and often wake up at night. Many children develop headaches, nausea and nocturnal enuresis; girls may develop vulvovaginitis. Blood tests often show increased eosinophils. Enterobiasis may be diagnosed on the basis of clinical symptoms and the presence of eggs of threadworms in smears taken from the perianal folds.

To obtain a smear, a match pointed as a spatula and dipped in a 1 per cent solution of caustic potash or caustic soda is used. The smear taken from the perianal folds is removed from the match with the side of a cover glass and placed on a slide after first mixing the smear with a drop of a 1 per cent alkaline solution. The drop is covered with the cover glass, and the preparation is examined under a low power microscope.

The hyponychial contents in cases of children are examined by the same method; these contents may often be found to contain eggs of threadworms.

Treatment of enterobiasis may also be administered by the old method, namely, with sublimed sulphur which is given in the following prescription:

Rp. Sulfuris depurati 0.5
D.t.d. N. 15
S. 2 powders 3 times a day (for adults)

The course of treatment is 5 days; the powders are taken 1 hour before meals.

In cases stubbornly resisting the action of sulphur, treatment is administered with an extract of male fern (*Extractum Filicis maris aethereum*). On the eve of the treatment the patient is given a saline laxative (25 g of magnesium sulphate). The following morning the patient is administered an enema and given, on an empty stomach, 2-2.5 g of male fern extract (in capsules of 0.25-0.5 g each); the capsules are taken one after another (in the course of 15 minutes). Two hours later the patient is given a laxative and a light breakfast. After a lapse of 10 days the course of treatment is repeated.

Since the preparation is toxic and a number of people are very sensitive to it, it is necessary to remember the contraindications (diseases of the liver and kidneys, gastric ulcers) and see to it that fats are completely excluded from the diet on the days of treatment, because the preparation freely dissolves in them and therefore accumulates in the organism; the diet is prescribed 1-2 days before the treatment.

The most effective treatment of enterobiasis is that with preparations of piperazine, including piperazine adipinate, piperazine sulphate and piperazine hexahydrate; all these preparations are very effective and may be recommended for therapeutic practice. The doses and schemes of treatment with these preparations are given in the section "Ascariasis".

In enterobiasis the preparations of piperazine are prescribed in the same doses and are administered in 2-3 cycles of 3-5 days each with 7 day intervals between the cycles; a strict observance of the hygienic regimen is required.

Strict observance of personal hygiene plays an important part in the *prevention* of enterobiasis; vegetables and fruit must be consumed only thoroughly washed in boiled water, the finger nails must be carefully trimmed (especially in children) and the hyponychial spaces must be kept clean; to avoid scattering eggs of threadworms in the external environment, it is necessary to wear drawers tightly fastened around the legs and to change them in the morning and in the evening.

Trichuriasis

The disease is caused by infestation with whipworms (*Trichuris trichiura*) which parasitize in the large intestine, mainly in the caecum and the vermiform appendix.

The female parasites are about 4-5 cm long, the males—2.5-3 cm. The anterior part of the parasite's body is elongated in the form of a hair, the posterior part is thickened; in males it is bent like a hook.

The eggs of whipworms can develop in the external environment if the temperature is sufficiently high. This explains the spread of trichuriasis mainly in southern countries.

Man becomes infested by swallowing mature whipworm eggs; in the intestine the swallowed eggs produce larvae which with their pointed anterior ends burrow into the intestinal mucosa. If many whipworms infest the organism, they cause marked disturbances in nervous activity and symptoms of colitis.

The clinical picture of trichuriasis is characterized by headache, diminished appetite, nausea and vomiting, often a semiliquid stool containing mucus, abdominal pain (epigastric region and caecum), salivation, general thinning, irritability, dizziness and even loss of consciousness, and muscular spasm. Some patients exhibit hypochromic anaemia, lymphocytosis and aneosinophilia in the blood.

The diagnosis of trichuriasis is based on the clinical picture and the results of laboratory tests (a repeated test of the faeces by Füllborn's method and the method of a native smear).

Trichuriasis is very difficult to treat. Usually osarsol (acetarsone) and heptylresorcinol are used. The former preparation is toxic and therefore must not be administered to children under 6 years of age and adults past 55 years of age.

Before instituting the treatment of trichuriasis the patient must be carefully examined, to exclude all contraindications (diseases of the liver and kidneys, circulatory insufficiency, active pulmonary tuberculosis).

Osarsol is taken in a dose of 0.25 g 4 times a day one hour before meals. The course of treatment is 5 days. If toxic phenomena (vomiting, abdominal pain, urticaria, albuminuria, greenish urine) appear, treatment with osarsol is immediately discontinued. In such cases it is necessary to wash out the stomach, give the patient a saline laxative and a 10 per cent hyposulphite (thiosulphate) solution in a dose of 1 tablespoonful 6-7 times a day.

Heptylresorcinol is administered in a dose of 1 g. On the eve of the treatment the patient is given a saline laxative (25 g of magnesium sulphate) after which he must take no food for 12 hours before the beginning of the treatment. The preparation is dispensed in pills of 0.1 g each; 12 of them are taken on an empty stomach, one after another at 5-minute intervals. The patient is given his

breakfast only 4 hours after the administration of the preparation. The same evening he is given a saline laxative.

During the treatment with osarsol or heptylresorcinol patients must not consume seasoned or acid foods (sauerkraut, tomatoes, pickles, horseradish, mustard, marinades, vinegar) since they are likely to evoke the toxic effects of these preparations.

In cases where the treatment with osarsol or heptylresorcinol fails to produce positive results another course of treatment is administered 4-6 weeks later.

Trichinosis

Trichinosis is a human disease caused by a special species of helminths and accompanied by a temperature reactions, sharp headaches and muscle pains, oedematous lids and puffy face. Man contracts this disease by ingesting pork containing the causative agent.

Aetiology and pathogenesis. Trichinosis is caused by small round worms—trichinae (*Trichinella spiralis*). The flesh of hogs infested with trichinae contains the cysts of the parasite. The trichinae are usually found in the muscles of the diaphragm and the intercostals. When such meat is consumed the cysts dissolve under the action of the digestive juices, and the parasites are released (Fig. 28). The trichinae are capable of implanting themselves in the intestinal wall. Penetrating deep into the intestinal wall through Lieberkühn's glands fertilized females release a large number of larvae which the blood flow carries to the muscles. The trichinae implant themselves in muscle fibres and produce considerable structural changes in them, destroying the fibrils and the sarcoplasm; subsequently a capsule

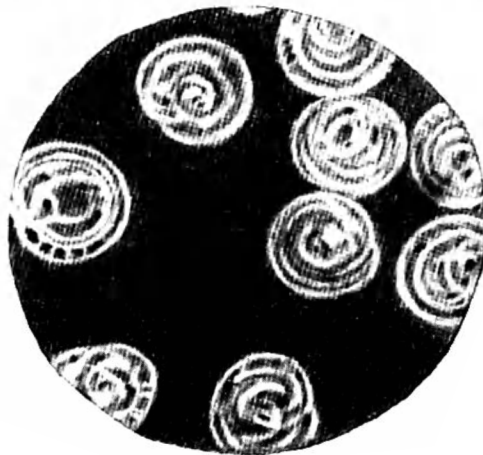


Fig. 28. Muscle trichinellae freed from cysts by the action of digestive enzymes

forms around each trichina and calcium salts are deposited in the capsule. The trichinae thus become encapsulated and, being reliably protected against unfavourable influences, may remain viable for several years.

Epidemiology. Trichinosis is contracted by ingestion of the flesh of animals infested with trichinae (mainly hogs).

As the result of systematic veterinary inspection and obligatory tests of hogs for trichinosis during their slaughter this disease now occurs much less frequently on the territory of the USSR than before.

Clinical picture. The incubation period is 10-25 days. The disease sets in gradually. During the first 2-3 days the patient complains of headache, general jadedness, dyspeptic phenomena (nausea, pressure in the epigastrium), photophobia and pain upon abduction of the eyes to either side.

From the third or fourth day of the disease the temperature rises to 38.5-39°C; the temperature curve is of an irregular type with disorderly rises and remissions. The febrile period is from 10 to 35-40 days and even longer.

In a number of cases pains appear in the gastrocnemius muscles, and the muscles of the arms and back; the pains become very intense; the appetite and sleep are disturbed. Some patients exhibit disorders of deglutition and speech as a result of affection of the lingual and pharyngeal muscles by the trichinae. Infestation of the diaphragmatic and intercostal muscles by a large number of trichinae may result in severe respiratory disorders.

Examination of a patient reveals a puffy face and oedematous lids. The changes in the blood picture are characterized by moderate leucocytosis (up to 8,500-11,000 leucocytes per 1 cu mm) with considerable eosinophilia reaching 20-55 per cent of the total number of leucocytes. The result may be fatal.

Diagnosis. Trichinosis may be diagnosed on the basis of epidemiological data (especially if the disease has attacked several persons who ingested the meat of the same hog) with due consideration of the gradual development of the disease, the temperature curve of irregular type, puffy face, oedematous eyelids, moderate leucocytosis and eosinophilia of the blood.

Treatment. During the first 2-3 days from the moment of the appearance of clinical symptoms it is recommended to give the patient 25 g of magnesium sulphate or some other saline laxative in order thoroughly to evacuate the bowels; this is followed by a 5- or 6-day course of treatment with *thymol*. This preparation is administered in a dose of 0.5 g 3 times per day in gelatin capsules which are punctured in several places by a pin in order that the preparation they contain may better be dissolved by the digestive juices. Sharp muscular pains are relieved by repeated administration of pyramidon and analgine (1-phenyl-2,3-dimethyl-5-pyrazolone-4-methyl-aminoethylene sodium sulphate).

Prevention. To prevent trichinosis requires careful and systematic control of the slaughter of hogs at slaughterhouses.

For this purpose in the laboratory of the slaughterhouse a microscopic examination is made of two specimens of meat taken from the crura of the diaphragm closer to the tendon. Twenty-four sections are made from the two specimens. If up to 5 trichinae are found in all the 24 sections, the carcass of the hog is boiled for 3 hours in slices not thicker than 8 cm, or is autoclaved and canned. If more than 5 trichinae are discovered, the meat is either destroyed or turned to technical purposes (manufacture of technical grease, glue, etc.).

In order to supply the consumers only with high-quality pork, every piece of it from the carcass subjected to trichinoscopy is stamped, while smoked pork (ham, bacon, etc.) is sealed.

Cestodiasis

Cestodiasis are morbid conditions caused by infestation of man with tapeworms (Cestoda). The characteristic morphological sign of these tapeworms is a flat body, consisting of separate segments (proglottids), absence of an intestine and hermaphroditism. The body of a cestode, depending on the species, is from 2-6 mm (for example, the tape form of the *Echinococcus*) to 10 m long (broad tapeworm—*Diphyllobothrium latum*).

The following basic parts are distinguished in the body of a cestode: a head (scolex), neck and body consisting of proglottids.

The human organism may serve as the intermediate or definitive host for the Cestoda. In the latter case the intestine of the human patient is parasitized by sexually mature tapeworms (beef tapeworms and broad tapeworms). In other cases the Cestoda parasitize in the human organism in their larval and sexually mature stages, for example, the pork and dwarf tapeworms. As an example of a disease in which a person infested by cestodes is only an intermediate host, mention may be made of *echinococcosis*.

Below are the main types of cestodiasis.

Taeniasis

The clinical picture, diagnosis and therapy of two diseases *Taenia saginata* infestation and *taeniasis* caused respectively by the beef (hookless) and pork tapeworms are very similar. That is why the two diseases are described in the common group of helminthiasis. *Taenia saginata* infestation is caused by the beef tapeworm which parasitizes in the intestine. A mature beef tapeworm is 5-8 m long.

Eliminated into the external environment in the patient's faeces the mature proglottids of the beef tapeworm (*Taenia saginata*) containing an enormous number of eggs contaminate the grass and water, which may lead to infestation of cattle with these tapeworms, the cattle serving as the intermediate host to this helminth.

On infesting cattle the larvae of the parasites develop in the intermuscular connective tissue. Man becomes infested by consuming half-raw or poorly-cooked infested beef.

Taeniasis is caused by infestation of man with the pork tapeworm (*Taenia solium*) which parasitizes in the intestine and reaches 1.5-2 m in length. The head of the parasite is supplied with 4 suckers and a rostellum with two rows of hooks. The body of the parasite consists of close to 900 proglottids.

The larvae of the pork tapeworm may parasitize in the organism of a hog (usually in intermuscular connective tissue) and of man. The latter may serve as both a definitive and intermediate host. Man becomes infested by consuming inadequately cooked or fried pork infested with the pork tapeworm.

Clinical picture. Taeniasis is marked by a number of not very characteristic pathologic nervous and gastrointestinal phenomena; these usually include apathy, adynamia, irritability, diminished working capacity, loss of appetite, headaches, nausea and vomiting, abdominal pains and intestinal dysfunction (constipation alternating with diarrhoea) and progressive anaemia. Sometimes taeniasis may simulate gastric and duodenal ulcers. Cysticerci form in the muscles and intermuscular tissue of hogs infested by eggs of the *Taenia solium*. When inadequately cooked or fried meat of an infested hog is consumed the cysticerci penetrate into the human intestine where they develop into mature pork tapeworms parasitizing in the small intestine. Man may be not only a definite, but also an intermediate host to the pork tapeworm.

Diagnosis. In diagnosing taeniasis it is necessary to consider the anamnesis (indications that the parasite's proglottids were eliminated in the patient's faeces), the character of the complaints and objective phenomena. The diagnosis must necessarily be confirmed by discovery of the parasite's eggs in helminthoscopic examinations of the faeces and in the smear from the perianal folds.

Treatment. Taeniasis and Taeniarhynchus infestation are treated with an extract of male fern (aspidium).

This preparation produces a toxic side effect, and it is therefore necessary to exercise considerable caution in using it. Diseases of the liver and kidneys, acute infectious diseases, gastric and duodenal ulcers, circulatory insufficiency and organic diseases of the central nervous system contraindicate treatment with male fern preparations.

Three or four days before the beginning of treatment with male fern preparations the patients are prescribed a diet of semiliquid, easily assimilable food (without fats). On the eve of the treatment patients are given a saline laxative (25 g of magnesium sulphate). The following morning (1 hour before administration of the preparation and necessarily on an empty stomach) they are given a cleansing enema.

The idea of the diet, laxative and enema is that the head of the parasite, deeply burrowed in the intestinal mucosa, is exposed by the thorough cleansing of the intestines, and the male fern preparation paralyzes its nerve ganglion and thereby renders the parasite harmless.

The male fern extract is administered in gelatin capsules in the morning (only on an empty stomach) over a period of 20-40 minutes. Adults are given 8-10 capsules containing 0.5 g of the preparation each. One hour after administration of the extract the patients take a saline laxative (25 g of magnesium sulphate). On the day of the treatment, as also during the preceding 3-4 days, the patients must not consume rich food.

The beef and pork tapeworms are eliminated in the patient's faeces within 5-6 hours. The treatment with male fern preparations is more effective in cases of *pork* tapeworm. It is necessary to watch out for the elimination of the parasite's head.

If the patient develops nausea in the process of treatment, he should suck on mint lozenges, drink lemon juice or swallow pieces of ice. In cases of marked poisoning with the extract (vomiting, cyanosis, diminished cardiovascular functions, liquid stool with blood) the administration of the preparation must be immediately discontinued, the stomach must be washed out, the patient must be given a saline laxative, must be kept warm (hot drinks, application of heat to the feet) and must be given a subcutaneous injection of ephedrine, cordiamine or camphor.

Prevention. Taeniasis can be prevented by thoroughly cooking or frying the meat consumed as food.

Diphyllobothriasis

Diphyllobothriasis in man is due to infestation with and parasitism of the broad tapeworm (*Diphyllobothrium latum*). According to its morphological characteristics, the parasite is a typical tapeworm (Fig. 29).

The parasite reaches a length of 2-15 m, its body numbering up to 4,500 separate proglottids.

Into the external environment the eggs of the parasite are eliminated in the faeces of infested man, hog or dog. Soon after the eggs have gained entrance into a water reservoir they give rise to larvae on which certain species of cyclops (minute crustaceans) feed. The fish, mainly pike, ruff and perch, which feed on the cyclops may become infested with the *Diphyllobothrium* and may subsequently infest man, if the latter consumes the inadequately cooked or fried flesh of these fishes.

In man the broad tapeworm parasitizes in the superior division of the small intestine by attaching itself to the intestinal mucosa by means of two bothriums (grooved suckers).

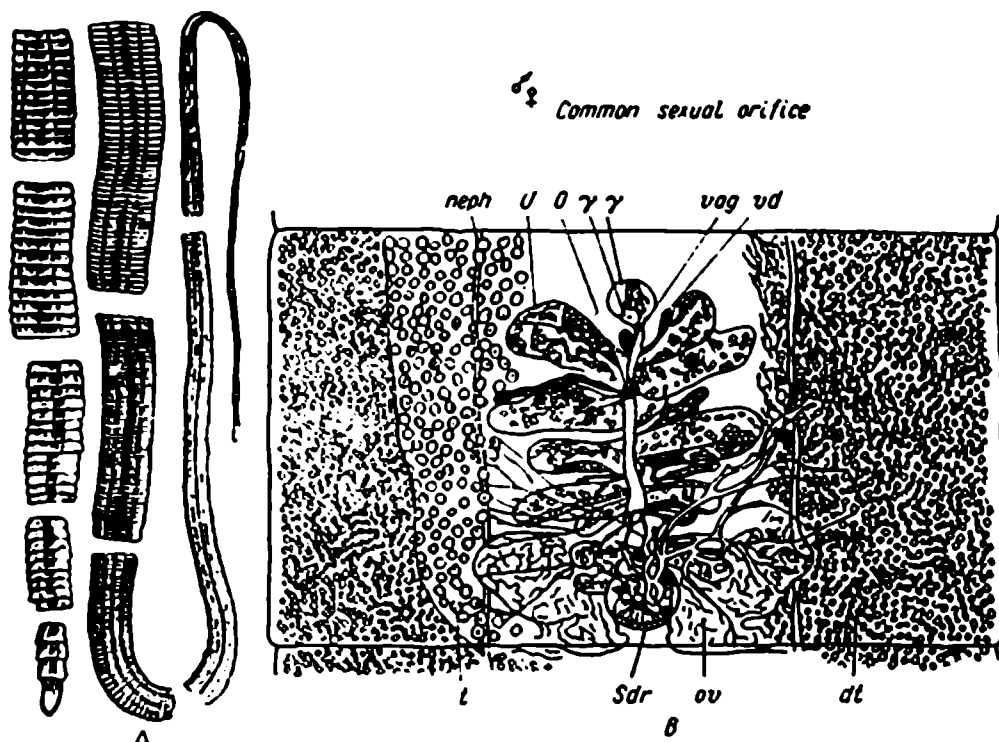


Fig. 29. Broad tapeworm (*Diphyllobothrium latum*). A—strobila (diminished); B—mature segment; O—uterine orifice; ov—ovaries; dt—yolk glands; Sdr—Mehlis gland; vag—vagina; u—uterus; t—spermaries; vd—ejaculatory duct; neph—trunks of excretory system

Clinically diphyllobothriasis is characterized by apathy, adynamia and anorexia, abdominal pain, anaemia and, not infrequently, eosinophilia. More severe cases are accompanied by pernicious-like anaemia (the colour index is above 1) which affects the bone-marrow haematopoiesis.

The disease is also marked by considerable pallor, oedema of the subcutaneous tissue, diarrhoea, functional heart murmurs and diminished gastric juice secretion.

Treatment of diphyllobothriasis begins with general roborants and antianaemic agents (preparations of iron, antianaemin [cobalt containing liver extract], campolon [aqueous liver extract], and repeated blood or erythrocyte-mass transfusions). Then, as in cases of taeniasis, patients are administered male fern extract (see "Taeniasis"). In connection with anaemia it is expedient to give the patients vitamin B₁₂.

General Prevention of Helminthiases

In the prevention of most helminthiases the most important part is played by sanitary protection of water reservoirs, the soil and foodstuffs from infestation with helminths and, primarily, from pollution with excrements of patients or intermediate hosts to the parasites. Extensive sanitary and hygienic measures in town and country, protection of sources of water supply, health education and inculcation of habits of personal hygiene are of decisive importance in the control of helminthiases.

The impurities must be decontaminated from the eggs of helminths in composts or by keeping them in closed pits with lime chloride (1 part of lime chloride to 4 parts of impurities). Systematic disinfection of toilets and cesspools with lime chloride is an important method of dehelminthization. Diphylllobothriasis can be prevented by adequate frying or cooking of the fish used as food. Rational control of trichinosis and taeniasis requires careful veterinary examination of the slaughtered cattle and hogs at slaughterhouses: trichinelloscopy of the carcasses of hogs is particularly obligatory.

An auxiliary role is played by thorough cooking of the meat (see "Trichinosis" above), its salting and freezing in accordance with the rules of food hygiene. It is necessary to reveal all helminthiasis patients. It is particularly important regularly to examine people for infestation with helminths, especially in organized collectives (kindergartens, children's homes, schools, workers of the food industry) and to carry out dehelminthization in hospitals with obligatory records of its effectiveness.

To prevent enterobiasis, it is necessary, in addition to the aforementioned measures, to trim the nails of affected children because retention of the parasite's eggs in the hyponychial spaces may result in repeated autoinfection.

The overall measures of helminthiasis control extensively carried out in the USSR and the problem of extermination of a number of helminths in all stages of their biological cycle, scientifically substantiated by Academician K. I. Skryabin, warrant considering the aim of eradicating many helminthiases on the territory of the USSR quite feasible.

The extermination of helminths is based on carrying out a complex of measures: ridding the human organism of the parasitic worms, destruction not only of the parasites driven out of the human bodies, but also of their eggs and larvae, and protection of people from new infestation by extensive sanitation of the water, the soil and all populated areas.

II.

TRANSMISSIVE (BLOOD) INFECTIONS

The distinguishing feature of the group of *transmissible* infections (the designation adopted on the proposal of Academician E. N. Pavlovsky) is their transmission from patients to healthy people through blood-sucking parasites (lice, fleas, sandflies, mosquitos, ticks) with the causative agents necessarily penetrating through the skin into the general circulation. This mechanism of transmission determines a number of clinical characteristics of the given group of infectious diseases and their designation in science as *blood* infections.

The causative agents of the infections of this group may be various microorganisms: rickettsiae, spirochaetes, filtrable viruses and protozoans. In the organism of the vectors the causative agents extensively multiply either by direct division or by going through a cyclic development. For example, the *Rickettsia prowazeki*—causative agents of louse-borne typhus—multiply by direct transverse division in the epithelial cells lining the wall of the intestine of the infected louse, whereas malaria plasmodia go through the sexual cycle of development in the organism of the *Anopheles* mosquito which is the vector of malaria.

The circulation of the causative agents of transmissible diseases in the blood determines a number of characteristic functional and anatomic changes in the different organs and systems (for example, universal affection of the small blood vessels in typhus patients).

Some transmissible diseases have *natural foci*, i.e., they spread only in certain geographical regions; this is associated with the biological characteristics of the vectors which can live only under definite natural conditions.

The number of infectious diseases described below (louse-borne typhus, mite-borne typhus, endemic or murine typhus and Q fever) belongs to the group of *rickettsioses*. The common distinguishing feature of these diseases is the ability of their causative agents (various strains of rickettsiae) to parasitize intracellularly and thereby cause a number of characteristic histological changes in the endothelium of the blood capillaries or in the cells of the alveolar epithelium.

CLASSIC EPIDEMIC (LOUSE-BORNE) TYPHUS

Classic epidemic typhus caused by *Rickettsia prowazeki* is a general acute infectious disease transmitted from a patient to healthy people through lice; it is characterized by predominant affection of the vascular and nervous systems, a typical temperature curve and a rash on the skin.

It is one of the varieties of a vast group of rickettsial diseases of man, which include endemic (murine) typhus, tick-borne typhus (North-Asian *Exodorrickettsiosis*) and Q fever.

Brief historical information. Descriptions of a mass incidence of diseases with the clinical picture of typhus are found already in the works of physicians of antiquity; later these diseases were reported in the writings on medicine in the Middle Ages and in modern times.

The clinical characterization of diseases, formed in the first half of the 19th century, made it possible in 1856 to establish the nosological independence of typhus and typhoid fever and to separate them from the indefinite group of febrile diseases. A big contribution to questions concerning the clinical aspects and pathology of typhus were made by such outstanding clinicians as S. P. Botkin in Russia, Liebermeister in Germany and Murchison in Britain.

The works of L. V. Popov (1875) demonstrated the existence of specific changes (granulomas) in the small vessels of the brain of people who died of typhus. In 1877 O. O. Mochutkovsky (Odessa) proved the presence of the infectious factor (causative agent) in the blood of typhus patients, and somewhat later G. N. Minkh suggested the idea about the role played by lice in the transmission of this infection.

Later the role of lice in the transmission of this infection was shown by the French scientist Charles Nicolle (1900). The works of H. T. Ricketts (USA), Prowazek (Chechia) and the Portuguese investigator da-Roja Lima established the most important characteristics of the causative agent (*Rickettsia prowazeki*). The classical research (1916-1921) of the prominent Soviet scientist I. A. Delyayevsky was consummated by an all-round description of the pathologic anatomy of typhus. Since 1916 laboratory diagnosis of typhus has used the Weil-Felix test. In 1939 Durand produced a typhus vaccine.

The biological properties of the causative agent, the epidemiology, pathogenesis and immunogenesis have been studied in detail, and the clinical aspects of the disease have been described in all their variants. Since 1950 antibiotics (synthomycin (chloramphenicol), levomycesin, biomycesin (chlorotetracycline), terramycin and tetracycline) have been successfully used in the treatment of typhus. In the USSR typhus has been eradicated.

Aetiology. The causative agent of the disease is the *Rickettsia prowazeki* which is a microorganism parasitizing in the cells of the endothelium of the blood capillaries. The rickettsiae are egg-shaped; sometimes they resemble dumb-bells. They are 0.8 μ long and 0.35 μ wide; they stain very well with azure-eosin.

Under natural conditions the *Rickettsia prowazeki* multiply in the cells of the endothelium of the patient's blood capillaries and in the epithelial cells of the intestines of the lice infected by them. The rickettsiae may be cultivated in pulmonary tissue of white mice and in the chorioallantois of the embryo of a hen's egg, which is utilized for the production of the Durand-Cox typhus vaccine.

Epidemiology. The only source of infection is a patient from the last two days of the incubation period till the 7th or 8th day from the moment of establishment of normal temperature after the end of the fever. Infection carrying has not been demonstrated.



Fig. 30. *Rickettsia prowazeki* in the intestine of the body louse (semischematic representation)

1—epithelial cell with *Rickettsia prowazeki* multiplied in it; 2—a mass of rickettsiae falling out into the lumen of the intestine from the epithelial cell at the moment of its rupture; 3—a mass of rickettsiae in the lumen of the intestine; 4—erythrocytes absorbed by the louse

The louse (mainly the body louse—*Pediculus corporis*) becomes contagious to healthy people only 4-5 days after sucking a patient's blood. During this period the *Rickettsia prowazeki* which have entered the digestive tract of the louse together with the blood of the patient multiply enormously after implanting themselves in the epithelial cells lining the intestinal wall (Fig. 30). When the number of rickettsiae becomes too large the epithelial cell bursts and the rickettsiae together with the excrements of the louse are eliminated to the exterior where they contaminate the skin and underwear of the person on whose body the

louse is parasitizing. By scratching the skin the person rubs the excrements of the insect into the site of the bite, the rickettsiae gain entrance into the person's organism and pass into the circulation. At that moment the incubation period begins. The patient is contagious from the last two days of the incubation period, all through the febrile period and for another 7-8 days.

There were extensive typhus epidemics in tsarist Russia, especially at times of crop failure, natural calamities and war. It is characteristic that as late as the 19th century typhus epidemics attacked European countries, and the number of victims of this disease often exceeded the losses suffered in military operations.

During 1918-1922 a typhus epidemic broke out and became enormously widespread in the young Soviet Republic which was fighting

back numerous interventionists at the time of the Civil War. Only the system of state anti-epidemic measures made it possible to stop the further spread of this infection.

Single cases of typhus with a predominantly mild and moderately severe course were observed after 1948; by their clinical course it was impossible to make sure whether they were primary or recurrent diseases.

Pathogenesis and pathologic anatomy. The rickettsiae pass from the excrements of the infected louse through the scratch, crack in the skin or the site of the bite into the human blood which carries them all through the organism. As intracellular parasites the rickettsiae attack the endothelium of the arterioles and capillaries where they cause characteristic histological changes. In addition to endovasculitides with formation of thrombi, destruction of small vessels, stases and haemorrhages are observed. Also characteristic are the specific typhus granulomas—clusters of cells—surrounding small blood vessels like muffs.

The foregoing vascular changes are observed in different organs and tissues, but are particularly pronounced in the medulla oblongata and other parts of the central nervous system, including the cerebral cortex (Fig. 31). This explains the clinical symptoms on the part of the nervous system, the circulatory disorders and development of meningoencephalitis, i.e., the factors which determine the most important manifestations of the disease.

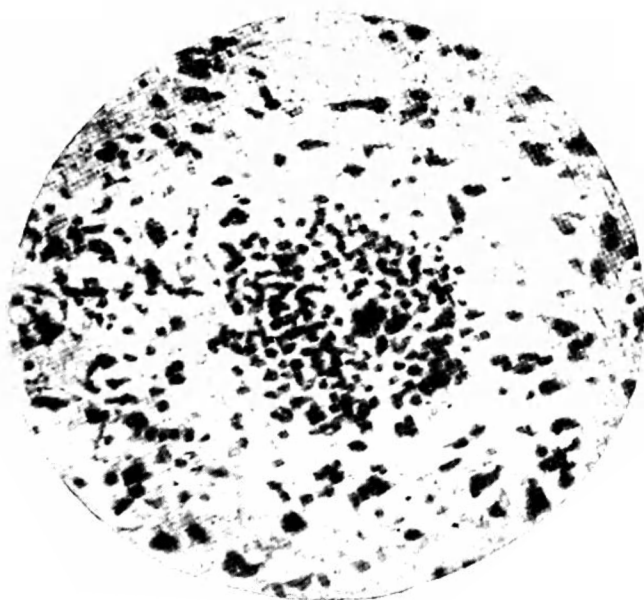


Fig. 31. Typhus. Granuloma surrounding a small cerebral vessel
(from A. I. Abrikosov and A. I. Strukov)

Analogous changes in the small blood vessels, supplying the ganglia of the sympathetic and parasympathetic nervous systems, disturb a number of vegetative functions, including metabolism and peripheral blood circulation.

The development of specific thromboendovasculitis and blood stases in the arterioles and capillaries explains the formation of roseolas and petechiae which appear between the fourth and sixth days of the disease.

All these disturbances in the patient's organism increase as a result of the specific intoxication caused by the metabolites of the causative agents, the toxins of the *Rickettsia prowazeki* depressing the activity of the nervous system and producing paresis of the blood vessels.

The toxins produced by the causative agent disorganize the blood circulation in the arterioles and capillaries of the typhus patient; this is particularly clearly pronounced in the central nervous system.

Clinical picture. The incubation period is from 6 to 23 days, averaging 10-14 days. The entire course of the disease is noted for a clear succession of appearance and disappearance of symptoms (cycles).

The disease sets in rather acutely, without prodromal phenomena or with a short (6-8 hours) period of prodromes manifested in general indisposition, jadedness and headache. This is followed by chills; the temperature begins to rise rapidly and reaches 38.5°C (in the morning) and 39.5 (in the evening) within 36-48 hours. It persists at this, or even at a higher, level for the following 7-9 days; at the end of the febrile period it falls by an accelerated lysis. The total duration of the febrile period is 10-11 days.

Since the clinical course of typhus is noted for a clear succession of increasing and diminishing symptoms (cycles) it is necessary, while observing the patient, to consider the period of the disease; this is important for diagnosing the disease and for administering treatment in due time.

During the first 3-4 days of the disease (before the appearance of the typical rash on the skin) its clinical picture is characterized by the following: the patient complains of a sharp headache, jadedness and insomnia. He is in a state of general excitement. Severe cases may be accompanied by clouded consciousness and delirium; the patient is excited and even aggressive and requires special watching, because typhus patients with a clouded consciousness sometimes attempt to leave the hospital, jump out of the window, etc.

In cases of moderate severity examination of the patient during the first 3-4 days reveals considerable hyperaemia and puffiness of the face, injection of the vessels of the sclerae (red, lustrous "rabbit" eyes) and the conjunctiva of the lids. It is important to emphasize that in typhus there are no inflammatory changes in the mucosa of the lids (conjunctivitis), but only an injection of the small blood

vessels which supply the conjunctiva. The retrotarsal fold of the conjunctiva sometimes exhibits minute haemorrhages (petechiae) which are particularly clearly seen when 1-2 drops of an (1 : 1,000) adrenalin solution are instilled in the eye. This diagnostic sign is known as the Chiari-Avtsyn sign. The hyperaemia and puffiness of the face are due to paresis of the vessels and their increased permeability resulting from affection of the regional (cervical) sympathetic nerve ganglia. Pressure on the roots of cervical nerves along the spine is often painful. The skin of the palms of the hands is sometimes slightly icteric. Respiration is usually accelerated. The pulse rate corresponds to the temperature level or is even somewhat higher (tachycardia).

Examination of the fauces often reveals an eruption on the mucous membrane (enantherma) and minute haemorrhages at the very root of the tongue. The tongue is dryish and evenly coated with a dirty-grey or brown film; later deep fissures may form on the tongue. The spleen enlarges moderately: from the fourth or fifth day this enlargement may be revealed by percussion and later by palpation. The liver begins to enlarge moderately between the fourth and sixth days. The stool is retained.

In connection with severe *bulbar* lesions (in nuclei of the medulla oblongata) some patients may exhibit the Godélier sign: they are unable to stick out the tongue beyond the teeth (result of lesions in the nuclei of the 12th pair of cranial nerves); the tongue seems to cling to the teeth (Fig. 32). Some patients may develop menin-



Fig. 32. Patient suffering from severe form of typhus with phenomena of meningococcal meningitis and marked bulbar disorders (6th day of the disease); the "tongue symptom" is particularly characteristic (see text)

goal phenomena (rigidity of the occipital muscles and Kerning's sign); severe, toxic cases are additionally accompanied by considerable encephalitic and bulbar phenomena, namely, impairment of articulation (dysarthria), choking, difficulty in swallowing (dysphagia), the aforementioned Godélier sign, and a masklike face. These symptoms are connected with lesions in the subcortical centres of the brain and in the nuclei of cranial nerves (phenomena of typhus encephalitis). Increased sensitivity (hyperaesthesia) of the skin is often observed.

The clinical picture during the first 3-4 days of typhus is characteristic in typical cases and makes it possible to establish the diagnosis or assume it with sufficient certainty. Attempts must be made to diagnose typhus during the first 3-5 days of the disease, before the appearance of the rash. If the patient is hospitalized and the focus is adequately disinfected and disinfected, no new cases are usually observed in the same focus, since the louse can transmit the infection only 5-6 days after sucking the blood of patients.

Once a rash has appeared on the skin on the 4th, 5th or 6th day of the disease it is no longer difficult to diagnose typhus.

It should be emphasized that the rash does not appear before the 4th or after the 6th day of the disease.

Typical cases of the disease are characterized by a polymorphous (heterogeneous in size and form) roseolous or roseolous-petechial rash which is localized mainly on the flexor surfaces of the arms and lateral surfaces of the trunk (Fig. 33); it is less abundant on the back and the medial surface of the thighs and shanks.

In very rare cases the rash is so abundant that it appears on the palms of the hands, the soles of the feet and on the face.

The inflammatory character of the changes in the small blood vessels in the region of the roseolas is confirmed by the fact that, if the skin in this region is stretched or pressed upon, the roseolas disappear because the blood is forced out of the vessels. The petechiae forming in the centre of the roseolas or outside of them are minute haemorrhages into the skin. The roseolas persist for about 4-5 days, then pale with a slight pigmentation and scaling of the skin at the sites of the eruption.

In typhus the capillaries become more fragile, which is established by means of the "pinch", "tourniquet" or "cupping" symptoms.

To produce the pinch symptom in a typhus patient, it suffices to pinch his skin on the chest; the result is an extravasation of blood; when a rubber tourniquet is applied to the patient's arm, minute haemorrhages appear below the site of application of the tourniquet. Numerous petechiae appear under a dry cup applied to the back or chest of a typhus patient.

At the height of the febrile period of typhus the blood picture is characterized by moderate neutrophilic leucocytosis (up to 9,000-11,000 leucocytes per 1 mm³) with a marked shift to the left (in

individual cases up to 35-40 per cent of band cells); the ESR is accelerated. From the 3rd-5th day of the disease the blood picture is also marked by aneosinophilia and relative lymphocytosis.

On the 8th or 9th day of the disease all pathological symptoms reach their maximum development: the blood pressure (both arterial and venous) is lowered, the tension of the pulse is diminished and the heart sounds are dulled; in some cases there is an extension of the percussion borders of the heart and a systolic murmur at the apex—signs of typhus myocarditis. The vascular system is affected the most; this is manifested in a lower tone of the vessels and their sluggish reaction to various external stimuli. Enlargement of the spleen and liver is discovered during the same period. Severe cases may be accompanied by profound delirium, motor excitement, tremor of the hands, hyperaesthesia, impaired hearing and meningoencephalitic phenomena, including speech and deglutition disorders. These phenomena disappear very slowly.

From the moment the temperature becomes normal the general condition of the convalescent in all cases of typhus considerably improves, the sleep becomes more tranquil, the appetite is restored and on the 7th or 8th day after the fall of the temperature the convalescent can already get out of bed. In cases treated with antibiotics the febrile period of the disease is considerably shortened; in children the disease runs a milder course.

In cases of a sufficiently complete clinical cure typhus convalescents may be discharged from the hospital 12 days after normalization of the temperature because by that time they are no longer contagious. This equally applies to patients treated with antibiotics.

The foregoing was a description of the course of typhus observed until 1948; since then the single cases of typhus have run a more favourable course and have been mainly mild or moderately severe cases.

As a rule, the intoxication has been moderate, and meningeal and bulbar phenomena have been very rarely observed. The patients have usually retained their consciousness, their rash has not been abundant and has consisted almost exclusively of roseolous elements; marked arterial hypotension and clinico-electrocardiographic indications of cardiovascular affection could be observed only in individual patients. The febrile period has been 10-11 days, and complications have been rare.

The reasons for the milder course of typhus in the single cases occurring since 1948 are considered above.

In patients immunized (inoculated) with a typhus vaccine the disease runs a still milder course and the febrile period is shortened to 7-8 days. The cases of typhus without a rash, which very rarely occurred in the past, may be diagnosed on the basis of the entire clinical picture with obligatory confirmation of the diagnosis by

means of the Weil-Felix test, an agglutination test with rickettsiae, and a complement fixation test; in these cases it is very difficult to establish a clinical diagnosis.

Complications. Of the possible complications of typhus mention must be made primarily of neurotrophic lesions in the tissues (necroses of the skin and bedsores) and thrombophlebitides (usually the veins of the lower extremities are affected). In some patients, especially in cases of preceding emaciation or poor oral hygiene, phlegmonous parotitis may develop. Sometimes circumscribed bilateral focal pneumonia develops; children may have otitides. Toxic neuritides of the acoustic nerve are not infrequent, although such patients soon completely regain the acuity of hearing (usually by the time they are discharged from the hospital). Typhus meningo-encephalitis develops in individual severe cases. An attack of the disease confers some immunity, and no relapses are observed. There is no proof that *the Rickettsia prowazeki* are retained in the organism of persons who have survived typhus. Recurrent attacks of typhus observed no sooner than 18 months after the primary attack are therefore always the result of reinfection. In the total typhus incidence a large share belongs to cases of recurrent infections.

Diagnosis. In diagnosing typhus it is necessary to consider the epidemiological data; it should be remembered, however, that in a number of cases it is impossible to establish the source of the infection, while the patient points out that he found no lice in his clothing or underwear. The failure to discover lice on the typhus patient in no way disproves the presence of this disease.

The main role in diagnosing typhus is played by the clinical picture of the disease; wherever possible it is necessary to utilize the epidemiological data.

Until the appearance of the characteristic rash on the skin it is difficult to establish the diagnosis, but the moment it appears the diagnosis is considerably facilitated. It should be emphasized that on the basis of sufficiently characteristic symptoms typhus may be diagnosed even before the appearance of the rash which becomes noticeable between the 4th and 6th days of the disease; in doubtful cases the patients must be referred to a hospital to ascertain the diagnosis as soon as possible; neutrophilia and a shift of the blood formula to the left are particularly typical.

The data of laboratory tests serve as confirmation of the diagnosis. The characteristic blood picture was described above.

The serological diagnosis of typhus is based on the positive results of the agglutination test with *the Rickettsia prowazeki* and the complement fixation test; the Weil-Felix agglutination test is less specific and sensitive and is made with a killed culture of *B. proteus* OX₁₉.

Before conducting the agglutination test the patient's blood serum is diluted in test-tubes with physiologic solution and 1 : 100,

1 : 200, 1 : 400 and 1 : 800 dilutions are prepared. Two drops of the killed culture is instilled in each test-tube and all the tubes are placed in a thermostat at 37°C for 20-24 hours. A 1 : 200 test titre and higher is considered demonstrative with due regard for an increase in the titre during a repeated test 3-4 days later. The Weil-Felix test may be conducted between the seventh and ninth days of the disease; if it is repeated at 2-day intervals an increase in the titre is usually observed.

It should be remembered that in persons inoculated against typhus or those who survived an attack of typhus and are at the time of the test suffering from another febrile disease the Weil-Felix test may prove positive (as anamnestic). In such cases it is of no specific importance and does not warrant the diagnosis of typhus.

If it is, for some reason or other, impossible to conduct the Weil-Felix test under the given local conditions, it is necessary to send a strip of cellophane with three separate dried drops of the patient's blood serum in an envelope to the nearest laboratory.

The agglutination test with a killed culture of the *Rickettsia prowazeki* is more sensitive and specific than the Weil-Felix test; it may be conducted already on the sixth or seventh day of the disease and it is positive in a greater number of cases than the Weil-Felix test.

If this test is conducted by the test-tube method, the laboratory confirmation of the diagnosis may be obtained as early as the 6th or 7th day of the disease, i.e., somewhat sooner than a positive Weil-Felix test. As a rule, the agglutination test with rickettsiae has rather high titres (1 : 800 and even higher) which increase upon repetition of the test every 3-4 days till the end of the febrile period. The minimum diagnostic titre is 1 : 100 with its subsequent increase.

The agglutination test with a killed culture of the *Rickettsia prowazeki* is strictly specific; it is the main method of laboratory diagnosis of typhus.

Of the methods of laboratory diagnosis so far proposed mention should be made of the *complement fixation test* for which a specially prepared antigen (suitable for the agglutination test) and the patient's blood serum (between the fourth and sixth days of the disease) are used. Being sufficiently specific and sensitive the complement fixation test may help to reveal atypical and effaced forms of typhus. Usually it is advisable to test a pair of serums taken from the patient at different periods of his disease. In persons who had typhus before, the reaction is produced at low titres and without their increase in paired serums. In typhus patients the titres of the complement fixation test usually continue to increase until the 12th-15th days of the disease.

The minimum diagnostic titre for the complement fixation test is a 1 : 200 serum dilution with complete arrest of haemolysis and

obligatory increase in the titre during repeated tests conducted at intervals of 4-5 days.

In establishing a *differential diagnosis* it is necessary to consider the period of the disease at which it is established; after appearance of the characteristic rash (the 4th, 5th or 6th day of the disease) the diagnosis is considerably facilitated.

During the first 3-4 days of the disease it is necessary to think primarily of influenza, measles, croupous pneumonia, and in some southern areas of the country—pappataci fever. It is often also necessary to differentiate the disease from typhoid fever, brucellosis, fresh cases of malaria and various rickettsioses (murine or endemic typhus, tick-borne typhus). The fundamentals of differential diagnosis are given below.

The most important symptoms of *influenza* are a short (2-4 days) febrile period, pains in the eyeballs and supraorbital arches, in some cases catarrhal phenomena in the nasopharynx and the upper respiratory tract, relative bradycardia and a characteristic haemogram (leucopenia with neutropenia and relative lymphocytosis); for greater details see Table 5.

Croupous pneumonia is characterized by pleural pains in the chest, dyspnoea, percussive and auscultative changes in the affected portion of the lungs, and scant discharge of heavy sputum of a rusty or sanguineous colour.

In the prodromal period *measles* is marked by rhinitis, coughing, photophobia, small areas of pityroid desquamation of the epithelium of the oral mucosa (Belsky-Filatov-Koplik's sign); an eruption in the form of large macules and, in some places, of merged elements appears on the face and then spreads in the course of 3 days to the trunk and lower extremities.

Typhoid fever sets in gradually, the temperature curve grows in stages, the skin of the patient is pale, bradycardia and a dicrotic pulse are observed; the tongue is oedematous and coated with a white film, but its edges and tip remain clear; the abdomen is inflated, and pain and rumbling are noted in the right iliac region on palpation. In a typhoid fever patient an eruption appears only between the 8th and 10th days of the disease in single regular round roseolous elements usually on the skin of the abdomen (Table 3). The blood shows leucopenia with aneosinophilia, neutropenia and relative lymphocytosis.

A positive haemoculture may be obtained during the very first days of typhoid fever and the Widal test becomes positive between the 8th and 9th days of the disease.

A differential diagnosis table of symptoms of typhus and typhoid and paratyphoid fevers is given below (Table 3).

Careful comparison of all clinical data and the use of laboratory tests make it possible to establish a differential diagnosis and correctly to diagnose each case of typhus.

Prognosis. In the cases of typhus observed since 1948 with a benign course and infrequent complications, the prognosis, as regards restoration of health and working capacity, has usually been favourable. Only in debilitated, emaciated patients, especially in elderly people, and in cases of serious complications, has the prognosis with regard to life and rapid restoration of working capacity been uncertain.

However, early rational treatment with synthetic antibiotics (tetracycline, levomycetin, biomycin) and simultaneous administration of agents supporting the cardiovascular function and eliminating intoxication make it possible to cure almost all hospitalized patients. Early (within the first four days) hospitalization of typhus patients with immediate institution of antibiotic treatment is an important therapeutic factor. The complications of the disease, especially thrombophlebitides, necroses of the skin and bedsores, as well as parotitides and otitides, may long hinder recovery and therefore require special care and in some cases appropriate surgical intervention. It is necessary to diagnose the complications in due time.

Treatment and care of patients. All typhus patients are subject to compulsory hospitalization in contagious departments of hospitals.

A clean bed with frequent changes of underwear and bed linens, a soft mattress and well ironed sheets not only provide the patient with the necessary comforts, but also prevent the development of bedsores; the underwear and linens must be changed as soon as they are soiled with the patient's excretions.

The patient's skin must be daily rubbed down with a towel moistened in warm water containing several drops of mint tincture. To prevent bedsores in the region of the sacrum and buttocks, on which pressure is exerted by the weight of the body, it is advisable to place a rubber ring under the patient. It is necessary to see to it that the patient should move his bowels regularly; in cases of constipation the patient must be given a cleansing enema. Owing to affection of the sacral division of the spinal cord (the nerve centres regulating the emptying of the bladder) severe cases of typhus may be accompanied by *ischuria paradoxa*, i.e., a condition in which the bladder is considerably dilated by urine, but the latter is either completely retained or is eliminated in drops (the dilation of the bladder may be established by percussion). In such cases a hot water bottle is applied to the lower part of the abdomen and the patient is given a warm enema; if these procedures fail, 1 ml of pituitrin is injected subcutaneously.

In exceptional cases, if it is impossible to stimulate evacuation of the bladder, catheterization is resorted to (Fig. 34); this procedure requires strictest asepsis, because introduction of coccal or other infection into the urinary tract may result in pyelitis, cystitis or even urosepsis.

Table 3

Typhus	Typhoid fever, paratyphoids A and B
1. Acute or subacute onset with a rise in temperature to 38.5-39.5°C during the first 1.5-2 days; during the following 7-8 days the temperature curve persists at the same constant level	1. Gradual onset with slow, stepped rise in the temperature curve to 38.5-39.5°C during the first 4-7 days; subsequently the temperature curve persists at this level and exhibits a tendency to fluctuate from about the 10th or 12th day
2. The patient is excited, but extremely debilitated. Severe forms are accompanied by meningeal syndrome	2. The patient is depressed, inhibited, indifferent to the surroundings and very sluggish (apathy, adynamia, depression of the nervous system)
3. The patient's face expresses excitement, it is hyperaemic and puffy, the eyes are lustrous, the vessels of the sclerae and conjunctivae are injected, the retrolarval fold of the conjunctiva often has petechiae (Chiari-Avitsyn symptom). Mild icterus of the skin on the abdomen is sometimes observed; herpetic eruption on the face is possible	3. The patient's face expresses indifference to the surroundings and is pale; all of the skin is pale and dry. Herpetic eruption is usually absent
4. The pulse rate corresponds to the temperature level or is even somewhat higher; relative bradycardia occurs as an exception	4. Characterized by relative bradycardia and dicrotic pulse; these symptoms are particularly typical of adults (mainly men)
5. Changes in the lungs are relatively rare	5. Diffuse bronchitides and focal pneumonias are observed in a considerable number of patients

6. The tongue is evenly coated	6. The edges and tip of the tongue remain clear and red, the rest of the surface of the dorsum of the tongue is coated. The tongue is usually edematous, and imprints of the teeth are therefore often found on its lateral surfaces
7. The abdomen is not inflated, the spleen is soft and enlarged, as revealed by percussion on the 3rd or 4th day of the disease, and is palpated between the 4th and 6th days of the disease	7. The abdomen is noticeably inflated, soft and painless on palpation; tenderness and rumbling revealed by palpation in the right iliac region, and sometimes shortened percussion sound (Padalka sign). The spleen is of dense elastic consistency, palpated from the 4th or 5th day of the disease
8. On the 4th, 5th or 6th day appears a polymorphous, rather abundant roseolous or roseolous-petechial eruption localized mainly on the lateral surfaces of the chest, the back and extensor surface of the arm; the roseolas are not sharply demarcated from the unchanged surrounding skin. The symptoms of the pinch, tourniquet and cupping are positive. Haemorrhagic eruptions and haemorrhages are possible	8. Roseolous eruption in the form of single regular round elements (about 2.5-3.5 mm in diameter) sharply demarcated from the pale skin; it is localized mainly on the abdomen; some of its elements are elevated above the surface of the skin. Haemorrhagic eruptions on the skin are very rare
9. The blood exhibits moderate leucocytosis, relative neutrophilia with a shift to the left (from the 3rd day of the disease)	9. The blood shows leucopenia, aneosinophilia, neutropenia and relative lymphocytosis
10. Serological tests (the Weil-Felix test, agglutination test with rickettsiae and complement fixation test) become positive on the 6th or 7th day of the disease	10. A haemoculture and a biliculture may be obtained on the first day of the disease; stool and urine cultures—between the 1st and 5th days of the disease. The Widal test is positive from the 8th-10th day of the disease in increasing titres

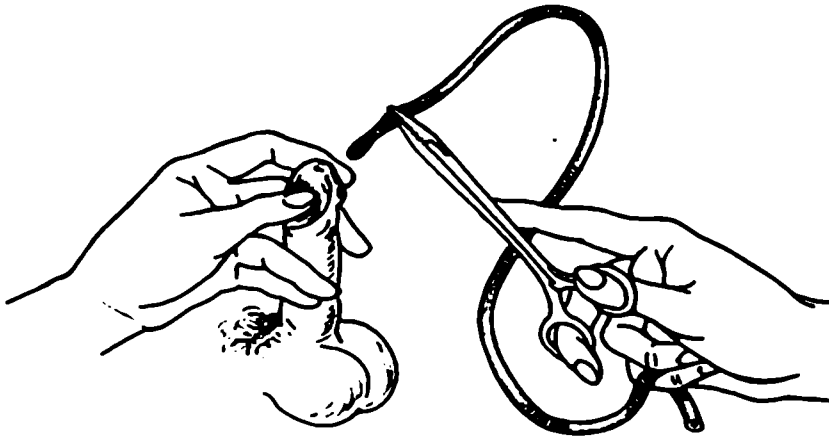


Fig. 34. Method of introducing rubber catheter

The patients must be more often turned in bed to prevent focal hypostatic pneumonia.

It is necessary to make the patients rinse their mouths after meals, in severe cases the attending personnel must swab the mouths of the patients with a cotton tampon moistened in a 1 per cent boric acid solution containing glycerin.

These simple measures prevent the development of phlegmonous parotitis which is sometimes due to penetration of the infection from the oral cavity through the parotid ducts.

Sharp headaches are relieved by application of an ice bag for 20 minutes with intervals of the same duration.

Unconscious, excited and aggressive patients must be kept under observation by a specially assigned nurse. Such patients must sometimes be covered with a hammock net tied to the bed.

The patients must be fed four times a day and be given a lot to drink. They require a good deal of vitamins, especially vitamin C (up to 800 mg of ascorbic acid per day) and vitamin B₁. The diet must consist of semiliquid, highly caloric and easily assimilable food: rice soup, liquid cereals with butter, jellies, steamed meat balls and quenelles, fresh boiled fish, fresh curds, acidophilous and sour milk, soft boiled eggs, caviar, stewed fruit and ground apples.

Antibiotics—levomycetin, biomycin, tetracycline or terramycin—are used in the treatment of typhus. Antibiotic treatment is continued until the second day (inclusive) of normal temperature. Patients treated with antibiotics improve rapidly; as early as the 2nd or 3rd day of the treatment the intoxication diminishes, the headaches abate and the temperature begins to fall, becoming normal from 2 to 4 days after the beginning of antibiotic treatment.

Treatment with preparations of the tetracycline series (biomycin, tetracycline and terramycin) is the most effective. As Fig. 35 shows treatment with biomycin leads to a rather quick normalization of the temperature. Biomycin, tetracycline or terramycin is administered per os in a dose of 300,000 U 4 times per day (until the second day of normal temperature, inclusive).

To support the cardiovascular functions, cordiamine is prescribed (20 drops 3 times per day); in cases of marked arterial hypotension patients are given subcutaneous injections of 0.6-0.8 ml of a 5 per cent ephedrine hydrochloride solution. In cases of milder cardiovascular disturbances cordiamine is prescribed (2 ml intramuscularly). Patients with a predominant affection of the myocardium are administered subcutaneously a 20 per cent oil solution of camphor in a dose of 2-3 ml 3 times per day.

In severe cases with marked general intoxication intravenous infusions of a 40 per cent glucose solution in doses of 30-40 ml or intravenous infusions (by the drip method) of a 5 per cent glucose solution in a dose of up to 600-800 ml are administered. Intravenous infusions, as well as subcutaneous administration, of physiologic solution are beneficial; mesaton (meta-oxyphenyl methylaminomethanol hydrochloride) or noradrenalin are administered for collapse.

To eliminate insomnia, patients are given hypnotics (barbamyl [amytal sodium], medinal [barbital sodium] and luminal); in cases

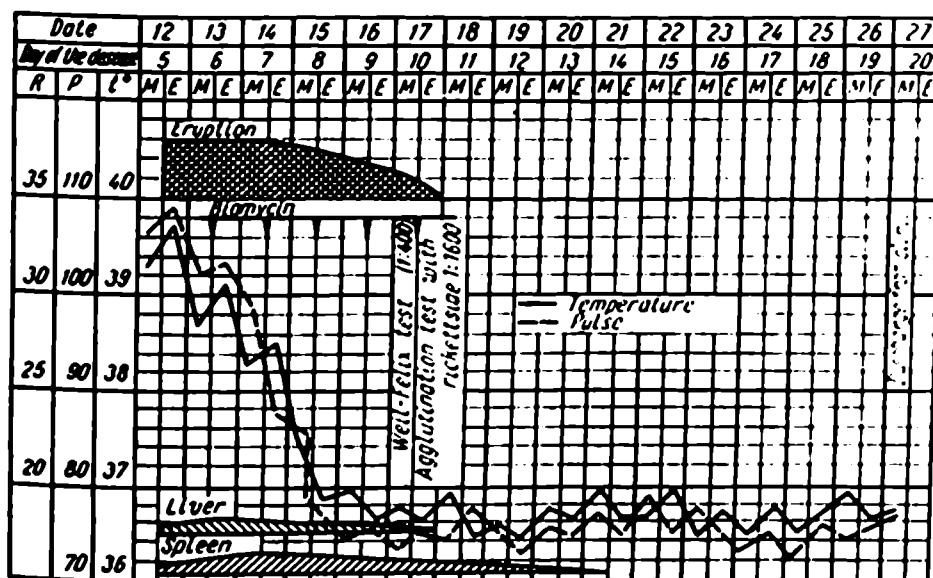


Fig. 35. Temperature curve of typhus patient treated with biomycin (300,000 U 4 times per day)

of considerable excitement promedole (4-phenyl-4-propoxy-1,2,5-trimethyl-piperidine hydrochloride) is administered.

In cases of purulent complications (otitis, parotitis) patients are given penicillin, and, if necessary, surgical intervention is resorted to. For trophic ulcers and bedsores injections of strychnine (1 ml of a 1 : 1,000 solution) are administered, as an agent which normalizes sympathetic innervation of soft tissues, up to 600,000 U of penicillin a day is administered intramuscularly, and dressings with Vishnevsky's ointment are applied to the ulcer surfaces.

For the treatment of thrombophlebitides which sometimes complicate typhus leeches are used (6 leeches along the affected part of the vein), and the patients are given neodicoumarin (3,3'-carboxymethylene bis/4-hydroxycoumarin) under prothrombin control, penicillin; dry heat is applied to the affected extremity which is placed in an elevated position. Such patients must be kept in bed for 3 weeks without fail.

Prevention. The district department of sanitation and the epidemiological station are notified immediately after hospitalization of a typhus patient. The apartment or hostel in which the patient lived is disinfected and an epidemiological examination is simultaneously conducted in the focus.

The patient's underwear and bed linens are boiled and washed in 5 per cent DDT soap, while his upper garments, blankets and mattresses are treated in disinfection chambers.

All persons living in the patient's immediate surroundings wash in a special bath, while their underwear, clothing and bedding are disinfected in the same manner as those of the patient.

All of the aforementioned measures must be carried out simultaneously and the disinfection in the focus must be repeated within 8 days.

Medical workers must daily take the temperature of all people living in the given focus over a period of 25 days after hospitalization of the patient and must additionally give them medical examinations every 3 days.

The persons who lived or were present in the typhus focus are kept under general clinico-epidemiological observation for 71 days from the moment of appearance of the first case.

An exceptionally important role in the control of typhus is played by its early diagnosis and hospitalization of the patients. As was already mentioned, a louse becomes contagious to healthy people only 4-5 days after it has sucked a typhus patient's blood. That is why, if a patient is hospitalized before the fifth day of his disease, a simultaneous, all round and repeated disinsection of the typhous focus is performed, and all the residents of the given apartment or hostel are administered sanitary treatment, it may be assumed that there will be no new cases of typhus in this focus. Practico has confirmed this assumption.

An auxiliary role in the prevention of typhus is played by inoculations with Durand's vaccine manufactured in the USSR by M. K. Krontovskaya and M. M. Mayevsky's method. The vaccine is a suspension of *Rickettsia prowazeki* cultivated in lungs of white mice; after grinding the pulmonary tissue of mice inoculated with *Rickettsia prowazeki* internasally, the tissue is centrifuged, in order to separate the particles of it from the rickettsiae, and the resultant pure suspension of rickettsiae is killed with formalin.

The vaccine is administered subcutaneously 3 times in doses of 0.5 ml, 1 ml and 1 ml at 6-day intervals. The immunity develops 3 weeks after the end of the inoculations and is effective for 8-10 months. Typhus incidence among immunized people is much lower, and in cases where the disease develops it runs a much milder course than in nonimmunized patients. However, when there are no epidemics, inoculations against typhus may be made to persons whose work exposes them to the danger of infection (the personnel of contagious hospitals, disinfectors, porters at railway and other transport depots, barbers, workers of delousing stations, etc.).

Another typhus vaccine is also used for immunization to typhus; this vaccine containing *Rickettsia prowazeki* killed with ether is likewise administered subcutaneously.

Overall anti-epidemic measures make it possible successfully to control the spread of typhus and sharply to reduce not only epidemics, but also the sporadic cases of the disease.

TICK-BORNE TYPHUS OR NORTH-ASIAN IXODORICKETTSIOSIS (RICKETTSIOSIS ASIATICA)

Brief historical information. Since 1938 a number of Soviet investigators (E. N. Pavlovsky, O. S. Korshunova, S. M. Kulagin, M. K. Krontovskaya and others) have studied the natural foci, epidemiology and most important properties of the causative agent of tick-borne typhus which is a rickettsial disease. The studies have been followed by deeper and more extensive observations of the clinical aspects of this disease.

The disease undoubtedly occurred at remote historical periods, but physicians have only recently gained knowledge of it.

Aetiology and epidemiology. Tick-borne typhus is caused by a special strain of rickettsiae—*Dermacentrozetus sibiricus*. Certain species of pasture *Ixodes* (parasitic ticks) and the species of wild animals (field mouse, gopher and hamster) which may be infected by these ticks are the reservoir of this infection in nature. Since the existence of *Ixodes* ticks and the wild animals which they infect is determined by certain local conditions, the disease is characterized by a *natural focus* and therefore occurs only in certain geographical zones.

Man becomes infected with tick-borne typhus when bitten by an *Ixodes* carrying rickettsiae (the causative agent of the disease).

Clinical picture. The incubation period is 3-5 days with possible variations of 2-7 days.

As a rule, the disease sets in acutely with chills and a rapid elevation of the temperature to 39.5-40°C. Prodromes of the disease are observed less frequently; the prodromal period is 1-2 days and manifests itself in general indisposition, jadedness and headaches. The febrile period is 8-12 days; at the end of it the temperature falls lytically over a period of 3-4 days.

A *primary affect* develops on the skin at the site of the tick bite; it is a small dense infiltrate covered with a brown necrotic crust and surrounded peripherally by a pink hyperaemic border. The primary affect is usually localized on the hairy part of the head, in the region of the upper shoulder girdle and on the neck, i.e., on the exposed parts of the body where the ticks bite. The primary affect is often accompanied by development of regional lymphadenitis with enlarged axillary and cervical lymph nodes. In some cases the primary affect is absent.

A polymorphous roseolous-papular *rash* on the skin is a characteristic symptom; minute haemorrhages (petechiae) may form in the centre of the roseolas at a later period of the disease.

The eruptions break out mainly on the chest, back and flexor surfaces of the arms, but may cover the entire trunk and also appear on the face, palms of the hands and soles of the feet. It should be emphasized that the rash persists all through the febrile period of the disease and even at normal temperature, often leaving the skin somewhat pigmented.

The entire febrile period is accompanied by headaches and muscular pains, particularly sharp in the small of the back, the pulse is slow compared with the temperature level (relative bradycardia) and the blood pressure falls. In some cases the liver and spleen are enlarged. The patient has a characteristic appearance, especially during the first 3-4 days: his face is hyperaemic, the vessels of the sclerae and conjunctiva of the lids are injected.

Towards the third or fourth day the blood picture is characterized by a slight neutrophilic leucocytosis (about 9,000-9,500 leucocytes per 1 mm³) with a moderate band-cell shift to the left; the ESR is accelerated to 35-45 mm/hr. These changes in the haemogram and the accelerated ESR persist till the end of the febrile period.

Diagnosis. The disease is diagnosed on the basis of epidemiological data (sojourn in an endemic area with a natural focus, tick bites), anamnesis, primary affect, clinical picture (with characteristic roseolous-papular eruption) and haemogram. An *agglutination test* (with a titre of at least 1 : 200) and a *complement fixation test* with a killed culture of *Dermacentor sibiricus* serve as a laboratory confirmation of the diagnosis.

Differential diagnosis. During the early period of its development

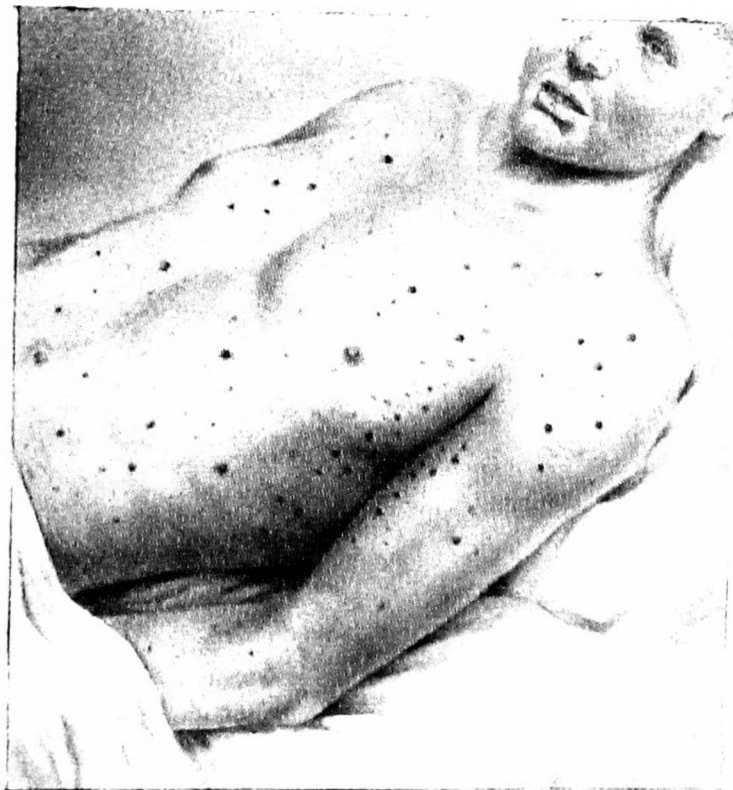


Fig. 33. Eruption in typhoid patient, 5th day of the disease, moderately severe case.

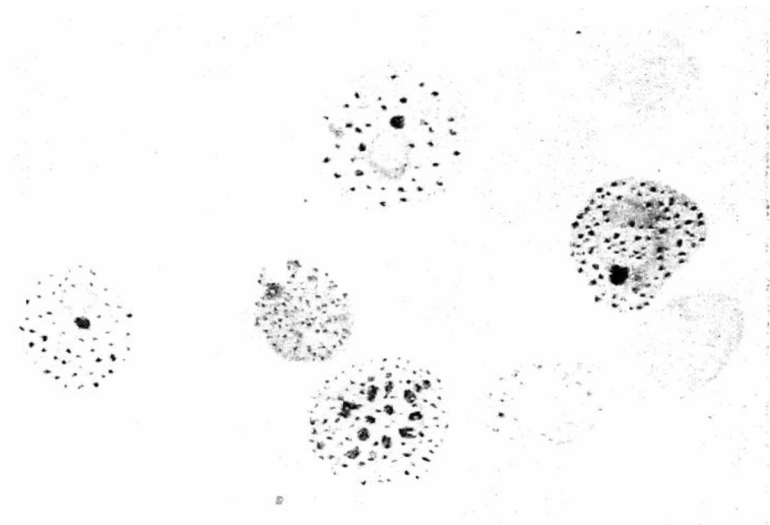


Fig. 45. Plasmodia of tertian malaria (schizonts)

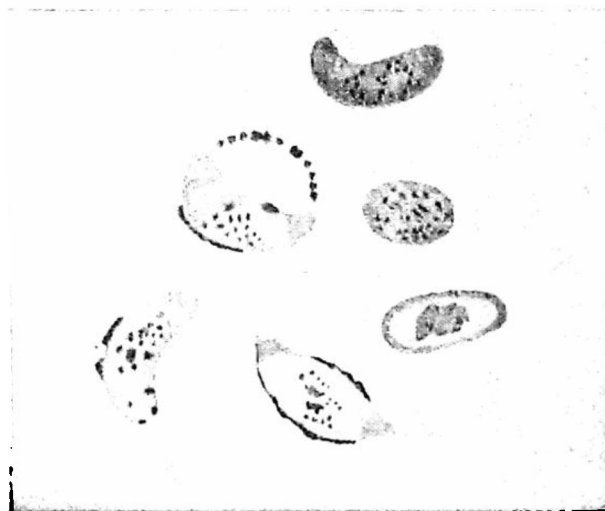


Fig. 46. Plasmodia of tropical malaria (gametocytes)

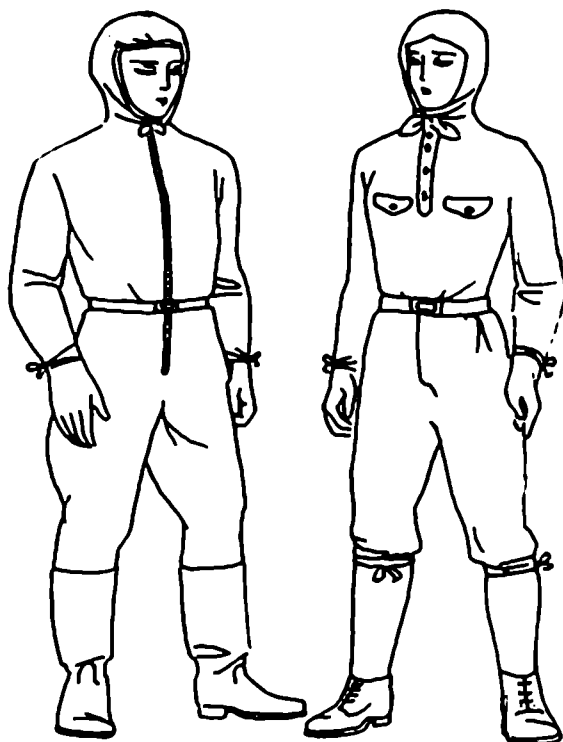


Fig. 36. Clothing worn for protection against tick bites

a—coveralls with hood; b—men's clothes adapted to wear for protection of the neck and head (drawing by N. K. Preobrazhenskaya)

the disease simulates a number of other infectious diseases, including *influenza*, *louse-borne typhus* and *swamp fever*.

The disease is treated with biomyacin (300,000 U four times per day). The patient must be given this preparation until his temperature has returned to normal and for two more days.

Good results are produced by treatment with tetracycline or terramycin; treatment with synthomycin or levomycetin is less effective.

All patients must be treated in a hospital; they require the same care as epidemic typhus patients. The disease runs a favourable course; complications are rare, although cardiac changes are possible.

Prevention. When settling areas where there are cases of tick-borne typhus it is necessary thoroughly to clear the plot allotted for dwellings, industrial or agricultural needs. The plot must be cleared of grass, shrubbery and fallen twigs, thereby depriving the ticks of the conditions of their natural habitat. Pasture *Ixodes* are the vectors of tick-borne typhus (tick-borne rickettsiosis); sometimes they parasitize on domestic animals, and it is therefore necessary

to dust these animals with hexachlorane (hexachlorocyclohexane) or DDT powders; these insecticides kill the ticks which have sucked in.

Individual protection from *the Ixodes* consists in wearing Pavlovsky's head nets, impregnated with a 10 per cent carbolic soap solution, and special coveralls (Fig. 36), boots and gloves. In endemic foci each person who has to be in areas inhabited by *Ixodes* must daily examine his body, underwear and upper garments, and must exterminate the ticks.

ENDEMIC OR MURINE RICKETTSIOSIS (ENDEMIC OR MURINE TYPHUS—RICKETTSIOSIS ENDEMICA MURINA)

Endemic or murine typhus is a rickettsial disease caused by *Rickettsia mooseri*.

Actiology. *The Rickettsia mooseri*—causative agent of the disease—are coccoid or rod-shaped, 0.2-0.3 μ wide and 0.7-0.8 μ long. In the organism of infected experimental animals they parasitize in the cells of the mesothelium. They multiply very well on the chorioallantois of the chick embryo.

Epidemiology. Rats are the reservoir of this infection in nature; owing to this the disease is closely connected with the spread of this rickettsiosis among rats. In large seaports where infection with endemic or murine rickettsiosis is possible it is necessary, in all unclear cases of febrile disease, to remember that there may be cases of this infection among the local population. Man contracts this disease from infected rats or from fleas parasitizing on these rats; man may also contract the disease by consuming water and food-stuffs infected with the urine of such rats.

Clinical picture. The incubation period averages 8-12 days. The symptoms of the prodromal period (early manifestations of the disease) consisting in general indisposition, headache and nausea are usually pronounced. These are followed by chills and rather sharp pains in the small of the back and a rise in temperature to 38.5-39.5 C. The febrile period with a constant-type temperature curve lasts 11-15 days; the temperature returns to normal by accelerated lysis (in 1.5-2 days). On the 6th or 7th, and sometimes even on the 5th day characteristic roseolous or roseolous-macular eruptions appear on the skin. The eruptions usually localize on the abdomen, back and extremities.

In some cases the eruptions are very abundant (Fig. 37).

Unlike epidemic typhus, in cases of endemic (murine) typhus the eruptions may appear even on the palms of the hands and the soles of the feet.

The course of the disease is generally favourable, no complications or relapses are observed, but the period of convalescence may take

up to 3 weeks (weakness, fatigability and poor appetite are observed).

The diagnosis is established on the basis of the clinical picture of the disease and the epidemiological data (sojourn in an area where there are cases of endemic typhus). In endemic typhus patients the Weil-Felix test may be positive from the 8th, 9th, or 10th day of the disease; a positive test is demonstrative in a 1:200 and higher titres. Since the Weil-Felix test is positive in both epidemic and endemic forms of typhus, these diseases may be differentiated by *laboratory data* only with the aid of an agglutination test with rickettsiae and a complement fixation test with the antigen of the *Rickettsia mooseri*.

Treatment. Preparations of the tetracycline series—biomycin, tetracycline and terramycin—are used in the treatment of this disease. One of these preparations is prescribed in a dose of 300,000 U four times per day until the temperature has returned to normal and for two more days. The therapeutic effect is quite satisfactory.

Prevention. The most important preventive measures include systematic extermination of rats in seaports and hindering rats from leaving ships arriving from foreign ports. To hinder rats from leaving ships, special devices are provided at moorings. Zinc phosphide is used as bait.

An important role in preventing endemic typhus is played by protection of foodstuffs and water sources from infection with the urine of rats which are the reservoir of this infection.



Q FEVER (Q RICKETTSIOSIS)

Q fever refers to a special rickettsial disease which is characterized by elevated temperature, often a sort of pneumonia, but no skin eruptions which are typical of most rickettsial diseases.

Historical information. An infectious disease occurring among slaughterhouse workers was described in Australia under the designation of Q fever (Q—short for *query*, implying doubt) in 1937. Subsequently this disease was observed in the USA, on the Mediterranean coast and in a number of different countries.

The causative agent of the disease—*Rickettsia burnetii* was isolated in 1939; the connection between this disease in man and in cows, sheep and goats was established later. The clinical picture, diagnosis and methods of treatment of Q fever have been studied quite exhaustively.

Aetiology. The disease is caused by *Rickettsia burnetii*, small microbes (2-2.5 μ long and 0.3-0.5 μ wide) occurring in pure culture as coccoid or rod-shaped cells; the *Rickettsia burnetii* are capable of producing filtrable forms which are well cultivated in chick embryos.

Epidemiology. Cases of Q fever have been recorded in various countries, including the USA, Britain, France, Italy, and the Balkans, particularly Greece and Turkey.

It should be remembered that cattle may be infected with Q fever in various areas, including the European part of the USSR, Transcaucasia, Central Asia, the Urals and Siberia, where single cases and sometimes epidemics of this disease may be observed. Accordingly, cases of Q fever are possible among people in various geographical zones.

Under natural conditions Q fever may affect cows, goats, sheep and, from time to time, birds and certain rodents. From these animals man contracts the disease through direct contact (occupational disease) and through certain species of *Ixodes* parasitizing on infected animals. In cows the infection with Q fever occurs without objective signs; the milk and urine of infected animals contain large numbers of the *Rickettsia burnetii*. People working with the wool of infected animals may contract the disease even if they are far removed from the zoonotic foci of infection. *Rickettsiae* may gain entrance into the human organism through bruises and scratches on the skin and by being inhaled with particles of dust.

Clinical picture. The incubation period averages 20 days with variations of 14-26 days.

The following basic forms must be distinguished: (1) cyclic (divided into acute and protracted), (2) septic, (3) acute pneumonic, and (4) subacute pulmonary.

The acute cyclic form described below is the most frequent.

In 65-70 per cent of the cases the disease sets in acutely with chills and a rapid rise in temperature which by the end of the second or beginning of the third day reaches 39.5-40 C; during the days immediately following the temperature persists at this level with temporary remissions.

The patients complain of intense headaches and less intense muscular pains (mainly in the gastrocnemius muscles), poor appetite, insomnia, nausea and considerable general weakness; arthralgias are observed in 10-15 per cent of the cases.

Both during the febrile period and after the fall of the temperature exhausting, often profuse sweating, which discomforts the patients mainly at night, is observed in 25-30 per cent of the cases.

It is important to note that in Q fever there are usually *no eruptions on the skin*; this circumstance is important in differentiating this disease from other rickettsioses which are, as a rule, accompanied by eruptions. Ephemeral roseolous or vesicular eruptions are observed only in 0.5-0.7 per cent of all cases.

The visible mucous membranes usually exhibit no appreciable deviations from normal. The vessels of the sclerae and conjunctivae are rarely injected. The cases observed by us did not show this sign; during the febrile period the patient's face was pale. The disease is often accompanied by pains in the joints. A mild hyperaemia of the fauces and in some cases loose tonsils are observed during the very first two days of the disease; the tongue is moist and somewhat coated with a white film. The pulse lags behind the temperature level, and the blood pressure is slightly diminished; in some cases (30-40 per cent) the liver and spleen are enlarged.

In cases of air-borne infection many patients exhibit pathologic changes in the lungs (Fig. 38), whereas in cases of enteral infection or penetration of the causative agent through the skin or mucosa no pneumonia usually develops.

In cases accompanied by pneumonia changes in the lungs begin to develop between the 2nd and 4th days of the disease; the patient begins to cough and discharges scant, semiliquid, foamy sputum sometimes rust-coloured or containing blood streaks; incon-



Fig. 38. X-ray picture of lungs at different periods of fever
a - 3th day of the disease; b - 8th day of the disease

stant pains in the side appear. There are very few physical signs: a dull tympanic sound with small babbling moist rales is determined in the posterior inferior parts of the lungs. Sometimes percussion and auscultation fail to discover any changes in pulmonary tissue despite definite roentgenological data. Roentgenoscopy and roentgenography reveal (mainly in the inferior lobes) a number of rounded, less frequently oval with irregular contours, dark foci of a pneumonic character; at the same time the lymph nodes of the mediastinum are enlarged. The pneumoniae are usually focal or interstitial; lobar affections are rare.

In cases accompanied by pneumonia the changes in the lungs persist even after the end of the febrile period.

Regardless of the varieties of Q fever the blood picture during the first three days of the disease is unchanged; later a very slight leucocytosis appears or a normocytosis is retained with a simultaneous change in the leucocyte formula.

Neutropenia with a nuclear shift of the formula to the left and a relative lymphocytosis are characteristic; monocytosis is possible. The ESR is accelerated to 20-25 mm/hr.

During the first 2-5 days the temperature rises to 39.5-40°C and persists at this level for 3-18 days with remissions to subfebrility lasting 1-2 days, after which it returns to normal lytically over a period of 2-3 days.

Thus the febrile period lasts from 8-9 to 23-25 days and even longer (Fig. 39).

In some patients Q fever may run a severe course, especially if it assumes a *septic* character (protracted temperature reaction, depression of the nervous and cardiovascular systems, enlargement of the spleen, and frequent complications). In most cases, however, Q fever runs a favourable course, but recovery may take 3-4 weeks and the patient's strength and working capacity may be restored slowly. An attack of the disease confers rather lasting immunity.

Diagnosis. Q fever is diagnosed mainly on the basis of the clinical picture and epidemiological data. Besides, it is necessary to use an agglutination test of a specific antigen (killed *Rickettsia burnetii*) of the patient's blood serum. This test may be performed only from the 11th-13th days of the disease and repeated at later periods. Usually the test is positive between the 15th and 17th days of the disease. A demonstrative titre of the test, to confirm the diagnosis, is at least a 1:40 dilution of the serum with a sufficiently intensive agglutination (+ + or more). This test may be used retrospectively since the increase in titres continues for 5-6 weeks after the attack of the disease. If a *Rickettsia burnetii* antigen is not available, a strip of celophane with a drop of the patient's blood serum may be sent to an appropriate laboratory.

A complement fixation test with a specially prepared antigen is the most precise method of laboratory confirmation of the diag-

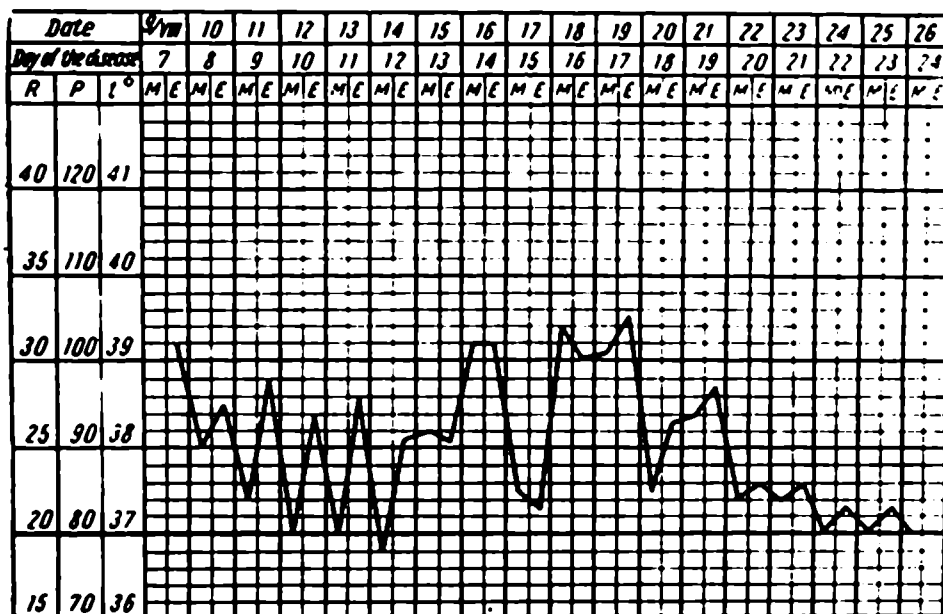


Fig. 39. Temperature curve of Q fever patient not treated with antibiotics

nosis. However, the test becomes positive only between the 10th and 15th days of the disease.

Differential diagnosis. Q fever must be differentiated from typhoid fever, brucellosis, ornithosis, miliary tuberculosis, pneumonia and sepsis of various aetiology. The diagnosis becomes completely authentic in cases of appropriate epidemiological, clinical and laboratory data with due regard for the various manifestations of the disease.

Treatment. All Q fever patients are subject to compulsory hospitalization and require the same care as typhus patients. The patients must be turned in bed more often, considering that many of them have specific pneumonia. With appropriate indications in more severe cases cardiovascular activity is supported by injections of ephedrine, cordiamine and camphor.

Good results are produced by biomycin or tetracycline (300,000 U four times a day for 5-6 days or even longer). Treatment with levomycetin (0.5 g six times a day for 5-7 days or even longer) is sufficiently effective, but when Q fever is treated with synthomycin or levomycetin the clinical phenomena disappear later than when treated with biomycin, tetracycline or terramycin.

Prevention The main measures aimed at preventing this rickettsiosis are revealment of animals infected with Q fever, veterinary inspection, health education and labour protection of people engaged in stock raising or wool processing, and systematic extermination

of *Ixodes* and *Argasidae*, the ticks which are vectors of this infection.

In areas where cattle is affected with Q fever only boiled milk should be consumed and caution should be exercised in working with wool.

A *Rickettsia burnetii* vaccine for inoculation against Q fever is now being elaborated. The vaccine is administered three times in doses of 0.25, 0.5 and 0.5 ml at 7-day intervals. Insusceptibility to the disease lasts about 1 year.

The Q fever focus requires epidemiological observation which may be discontinued only if no new cases of the disease have been observed for 25 days.

RELAPSING FEVER (TYPHUS, SIVE FEBRIS RECURRENS)

Relapsing fever is an acute general infectious disease characterized by an epidemic spread and transmission through lice; it occurs in the form of recurrent attacks connected with the entrance of masses of spirochaetes (causative agent—*Spirochaeta obermeieri* or *Borrelia recurrentis*) into the blood; the attacks gradually become shorter and are separated by gradually increasing periods of normal temperature. The disease is marked by an acute onset, high temperature, considerable enlargement of the spleen and sharp pains in the gastrocnemius muscles.

Aetiology. The disease is caused by special spirochaetes circulating in the blood of the patients. The spirochaetes were described by Obermeier in 1837; they have a form of a thin spiral and are 10-30 μ long and 0.2-0.5 μ thick; the spiral has 4-10 coils; its ends are often pointed. The spirochaetes possess considerable motility and perform active translational movements by rotating about their own axis; they can also bend at an angle to their axis.

During an attack of fever the spirochaetes may be seen under a microscope in a thick drop of the patient's blood stained with any aniline dye, for example, fuchsin or methylene blue. The spirochaetes are always located outside erythrocytes singly (Fig. 40) or in clusters; the latter is more frequently observed towards the end of the febrile period when the spirochaetes become agglutinated.

Actively moving living spirochaetes may be observed in a drop of the patient's blood under dark field illumination (in a microscope with a special condenser).

In addition to the patient's organism the spirochaetes may exist and multiply in body lice which are vectors of the disease.

Epidemiology. Under natural conditions relapsing fever occurs only in man, and the role of the source of infection may therefore be played only by a patient, especially during the febrile period, and a convalescent as long as he is contagious (about 15-17 days). The infection is transmitted by a patient to a healthy person

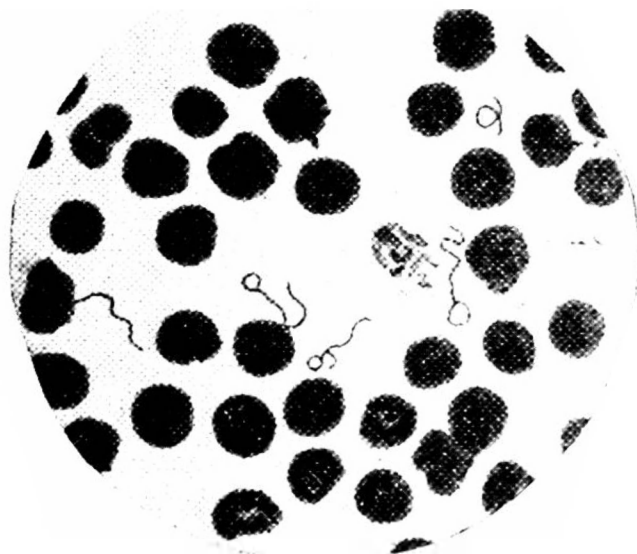


Fig. 40. Relapsing fever: Obermeier's spirochaetes (*Borrelia recurrentis*) in the patient's blood

through lice, mainly body lice. The louse becomes contagious only 4-5 days after sucking the blood of a patient during an attack of relapsing fever; this period is necessary for the spirochaetes to multiply in the inner cavity of the body of the louse, which contains a so-called celomic fluid. It has been established that the salivary glands and excrements of infected lice contain no spirochaetes. A healthy person is infected not through a bite of a louse, but through the crushing of an infected louse or severance of one of its legs when the celomic fluid containing a larger number of spirochaetes pours out on to the surface of the skin and then penetrates into scratches, bruises or other skin defects (microtraumas). Having thus gained entrance into the human organism the *Spirochaeta obermeieri* soon penetrate into the general circulation, at which moment the incubation period of the disease begins.

The contagiousness of the patient's blood, i.e., the presence of the causative agent in it at the height of the febrile period, was demonstrated as early as 1874 by G. N. Minkh who injected the blood of a relapsing fever patient into his own body and six days later, i.e., at the end of the incubation period, went down with a severe form of the disease. In 1881 this heroic experiment of auto-infection was reproduced by I. I. Mechnikov. The role of lice in

spreading the infection was demonstrated later (in 1912-1914 by C. Nicolle, Blezault and Conceill).

Less than 100 years ago the relapsing fever incidence was very high in various European countries; a number of severe epidemics of this disease was recorded in the course of the 19th century. In the past, relapsing fever epidemics were observed in connection with wars, economic dislocation and migration of people, which contributed to congestion and infestation with lice.

In prerevolutionary Russia relapsing fever was not a rare disease; from time to time the country was afflicted with extensive epidemics. After a considerable rise in its incidence during 1918-1922, the latter was soon reduced to single cases owing to measures persistently carried out by the Soviet public health services. The disease was completely eradicated on the territory of the USSR several years ago.

Epidemics of relapsing fever and typhus may develop simultaneously, but the more complex mechanism of infection with the former explains its lower general incidence and earlier cessation than those of typhus.

Pathogenesis and pathologic anatomy. Soon after penetrating into the human organism through various defects in the skin the *Spirochaeta obermeieri* enter the general circulation by which they are carried all through the organism. During the incubation period a large number of the spirochaetes remain in the central nervous system and the spleen where they may multiply. Invasion of the blood flow by large numbers of spirochaetes gives rise to an attack of fever with all its clinical manifestations.

The spirochaetes are capable not only of damaging the endothelium of capillaries with resultant embolisms and thromboses (usually with development of splenic infarctions), but also of deeply implanting themselves in the tissues. During apyrexia the patient's blood contains very few spirochaetes, although they persist in the central nervous system and the bone marrow.

There is as yet no general agreement concerning the reasons for the development of *recurrent attacks* of relapsing fever. There have been attempts to explain the recurrence of the attacks by the cycle of development of the spirochaetes, but the explanations lack the necessary substantiation. Soviet investigators (V. M. Aristovsky) have shown that during the first attack of relapsing fever the antigenic pattern of the spirochaetes changes and the immunity formed with regard to the first race-generation—of the spirochaetes is not effective with respect to the following generations. Only as the result of successive destruction of spirochaetes and formation of nonspecific immunity can man finally rid himself of the disease. The development of recurrent attacks is greatly stimulated by the fact that between the attacks spirochaetes not only persist in the central nervous system, but also multiply there and then pass into



Fig. 41. Relapsing fever. Spleen with miliary necroses and infarcts

the general circulation. Relapsing fever may be produced experimentally by infecting monkeys.

The *pathoanatomic changes* studied mainly in the past, before the use of antibiotics and arspenamine preparations are for the most part characterized by the following.

A dissected spleen appears dark-red, hyperaemic and considerably enlarged. Its pulp shows marked proliferation of cells and frequently necroses and infarcts (Fig. 41).

Histological examination of the liver reveals phenomena of mild parenchymatous hepatitis and sometimes small foci of necrosis. In severe cases of relapsing fever, especially in cases involving *bilious typhoid*, the changes in the liver and kidneys (diffuse nephritis) may be very serious, even to the point of severe degeneration.

Clinical picture. The incubation period averages 6-7 days. The clinical symptomatology of relapsing fever is quite characteristic. The disease sets in suddenly, acutely, with strong, often enormous chills, sharp headache and sometimes vomiting.

These phenomena are followed by intense muscular pains, mainly in the gastrocnemius muscles and the small of the back. The gastrocnemius muscles may be so sensitive that even the slightest contact produces intolerable pains.

In 6-8 hours (less frequently in 1-2 days) the temperature rises to 40.5-41.5 C. During the first attack it persists at this level with very slight daily variations and at the end of the attack falls critically to subnormal figures.

The very first days of the disease are marked by considerable weakness, appetite disturbances and insomnia. Examination of the patient reveals that his skin is somewhat icteric, dry, hot to touch and sometimes hyperaesthetic. In some cases small roseolas may appear on the fourth or fifth day of the disease; the roseolas last

but a few hours and then entirely disappear with a slight desquamation of the skin.

Relapsing fever is often accompanied by nasal haemorrhages due to increased permeability of the blood capillaries and mucous membranes, decreased number of thrombocytes and diminished blood clotting. The nasal haemorrhages are fostered by dystrophic changes in the parenchyma of the liver.

During attacks the patient's respiration is considerably accelerated (30-32 per minute). The attacks are characterized by tachycardia, the pulse rate reaching 130-140 per minute. The blood pressure falls moderately, and the heart sounds are somewhat dull.

Gastrointestinal function is disturbed. This was observed by experienced clinicians as early as the middle of last century. Constipation often changes to diarrhoea. The tongue is evenly and quite heavily coated with a dirty-white film; later it becomes dry and coated with a brown film.

Percussion shows the spleen to be enlarged already on the second day of the disease; on the 3rd or 4th day the spleen can be palpated; usually it projects 3-4 cm from under the left costal border. Sometimes the spleen is so enlarged that its inferior pole reaches the level of the navel. It enlarges in 65-85 per cent of the cases. Palpation of the spleen is painful owing to the dilation of its capsule. There have been cases of spontaneous rupture of an extremely enlarged spleen. The liver does not enlarge so much, but in many cases it projects 2-3 cm from under the costal border and is somewhat painful on palpation.

During febrile attacks the patients are often extremely excited and their sleep is, as a rule, disturbed.

During the first attack, especially towards the end, the blood exhibits moderate hypochromic anaemia; the changes in the leucocytes are more characteristic and are manifested in leucocytosis (10,000-12,000 leucocytes per 1 cu mm) with a shift of the leucocytes to the left. The ESR is, as a rule, quite fast (30-35 mm./hr) and becomes even faster during recurrent attacks.

The first attack usually lasts 6-7 days, but may vary from 3 to 8 days (Fig. 42). It usually terminates in a sharp, critical fall of the temperature to normal or, most commonly, to subnormal figures; during the fall of temperature the patient sweats profusely. The critical fall of temperature causes serious changes in cardiovascular function (to the point of collapse) and considerable general weakness, but several hours after the fall of the temperature the patient's condition becomes quite satisfactory. As soon as the temperature has returned to normal an interparoxysmal period (apyrexia) begins; this period lasts 5-7 days. During the first 2-3 days of this period the patient must stay in bed despite the fall of the temperature and general improvement of his condition.

The period of apyrexia is followed by another attack of the dis-

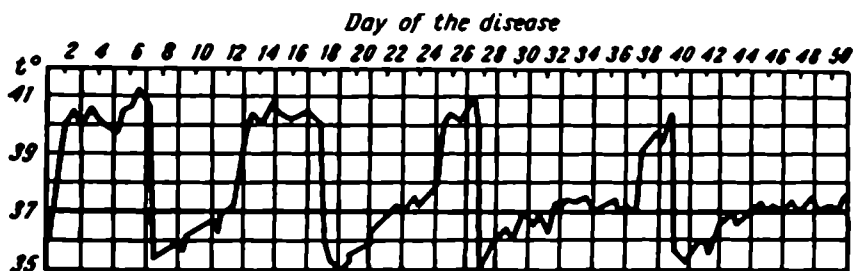


Fig. 42. Temperature curve of relapsing fever patient

ease. The symptoms of the attack are a sharp cold fit, headache and rapid elevation of the temperature to 39.5-40.5 C.

In some cases (12-15 per cent) relapsing fever may be limited to a single attack of fever accompanied by a marked clinical picture of the disease. Usually, however, there are three attacks. Each successive attack is shorter and the intervals between the attacks are longer.

In some cases there are 5-6 attacks with the febrile periods lasting 1-2 days and mild clinical phenomena.

To find spirochaetes in the blood during apyrexia (especially during the first apyrexia), the patient may be administered subcutaneously 0.8 ml of adrenalin (1:1,000) or given an intravenous injection of 0.3 g of novarsenol (neoarsphenamine), which *provoke* a temporary (16-20 hours) attack of the disease with appearance of spirochaetes in the blood. The spirochaetes are easy to find in a fuchsin-stained thick drop or in a smear of the patient's blood.

During the febrile periods the temperature curve is constant, although in some cases its constancy may be interrupted, the temperature falling to normal—so-called false crisis.

The clinical course of relapsing fever depends on the patient's age; the disease runs a more severe course in elderly and old people than in children.

In pregnant women, especially during the second half of pregnancy, and in persons with dystrophy relapsing fever often runs a severe course. Owing to the danger of abortion it is necessary to begin treating pregnant women affected with this disease as early as possible with massive doses of penicillin.

Complications. The course of relapsing fever, especially if the disease is untreated or treatment was instituted late, may become aggravated by concurrent pathologic changes in various organs and systems produced by the causative agent of the disease or by secondary microflora.

The recurrent nasal haemorrhages, sometimes very copious, are due to increased permeability of the blood capillaries and to thrombocytopenia.

During the febrile period the patient is in danger of developing acute vascular insufficiency (collapse) which requires urgent therapeutic measures: intravenous infusions of physiologic solution and glucose and subcutaneous injections of ephedrine and cordiamine.

The spontaneous rupture of an extremely enlarged spleen, observed as a rare complication, is accompanied by sharp pain in the region of the spleen, the patient becomes extremely pale, the pulse grows weak and the blood pressure considerably falls. The only chance to save the patient in such catastrophic cases is immediate surgical intervention (splenectomy).

Development of *splenic infarct* causes pains in the left hypochondrium, increased neutrophilic leucocytosis and faster ESR. Later, with the development of perisplenitis, prolonged auscultation through a phonendoscope applied to the region of the spleen reveals the sound of friction produced by the capsule of the spleen. In some cases splenic infarcts may suppurate.

As for the kidneys, diffuse nephritides running a severe course are now and then observed; protracted haematuria is also possible.

The possible complications of relapsing fever include iritides and iridocyclitides, opacity of the crystalline lens, keratitides and haemorrhages into the retina.

In childhood the disease may be complicated by suppurative otitis.

Patients of various ages may develop diffuse bronchitides and focal pneumoniae.

During the past epidemics of relapsing fever some patients had an extremely severe complication known as *bilious typhoid*. It may arise at the end of the first or, more commonly, at the end of the second attack of the disease. The development of choleraic typhoid sharply aggravates the patient's general condition, the headache grows more intense and a typhoid state develops. The pains in the small of the back and in the gastrocnemius muscles become particularly intense.

If the temperature was normalized before the development of choleraic typhoid, it rises very high with the onset of this complication. The skin and sclerae assume a visible icteric colouring. The liver and spleen become enlarged, the stool is usually retained, the tongue becomes dry, and the patient has skin and frequently copious nasal haemorrhages. The consciousness is clouded and the patient is often excited. In some cases choleraic typhoid may lead to death.

The pathogenesis of choleraic typhoid is due to an addition of secondary salmonellar infection (with bacteria of paratyphoids N₁ and N₂) which runs a septic course. This was established by the well-known Soviet infectious disease specialist G. A. Ivashentsov as early as 1921.

The usual course of relapsing fever may be aggravated by development of meningitis; affection of the peripheral nervous system may give rise to protracted neuritides.

Prognosis. Instituted in due time and vigorously administered treatment of relapsing fever ensures recovery in almost all cases. In the past, however, for example, during the 1920-1921 epidemic, when chemotherapeutic preparations were either absent or were insufficiently used, mortality reached 15-17 per cent.

It should be remembered that even with the modern methods of treatment old age, emaciation and various complications render the prognosis more serious, require the closest watching of the patients, vigorous therapy and considerate care. An attack of the disease does not confer adequate immunity, and recurrent attacks are possible as a result of reinfection.

Diagnosis. Relapsing fever can be diagnosed on the basis of epidemiological data (incidence of the disease in the area where the relapsing fever patient lived for 3 weeks from the onset of his ailment) and a careful analysis of the clinical picture of the disease.

It is particularly important to consider the following symptoms: acute onset of the disease with a cold fit and rapid rise in temperature to very high figures (40.5-41.5 C), headache, sharp pains in the gastrocnemius and other muscles, early enlargement of the liver and particular enlargement of the spleen, neutrophilic leucocytosis with a shift to the left, and recurrent nasal haemorrhages.

The laboratory diagnosis of relapsing fever during the febrile period of the disease is based on discovery of spirochaetes in fuchsin-stained thick drops of the patient's blood and their subsequent microscopy.

Living spirochaetes may be observed in the patient's blood under dark field illumination with a special condenser.

To find spirochaetes in the patient's blood during apyrexia, the following method elaborated by the Soviet microbiologist F. G. Berngol is used: 10 ml of the patient's blood is taken into a test tube from the ulnar vein and allowed to coagulate. Then the serum is drawn off into a centrifuge test-tube and is centrifuged for 45 minutes at 3,000 rev/m. This leaves on the bottom of the test-tube a precipitate which by means of a Pasteur pipette is transferred together with a little of the same serum to a slide, and a thick drop is prepared. After the drop has dried in the air it is fixed by Nikiforov's mixture (equal amounts of alcohol and ether) and stained with Ziehl's fuchsin solution (in a 1 : 10 dilution with distilled water).

In the beginning of the first febrile attack of relapsing fever it is necessary to establish a differential diagnosis with typhoid fever, typhus, malaria, brucellosis, croupous pneumonia and influenza.

In most cases it is possible correctly to diagnose relapsing fever by taking the epidemiological and clinical data into consideration and using laboratory diagnostic methods. In all unclear cases suspected of this disease it is necessary repeatedly to test for spirochaetes thick drops stained with fuchsin or methylene blue.

Treatment. Relapsing fever began to be treated with arsenicals, at first with atoxyl and arsacotin and then with salvarsan, as early as 1908. Neosalvarsan (neoarsphenamine) began to be used for the same purposes in 1912; this preparation is analogous to novarsenol which is now used in the USSR for the treatment of various diseases.

Novarsenol is used the most. It is administered in doses of 0.45-0.6 g to men and 0.45 g to women. The dose of novarsenol is dissolved in *10 ml of twice distilled water* and is immediately slowly (over a period of 2-3 minutes) infused into the ulnar vein.

After an intravenous infusion of novarsenol during a febrile attack the temperature begins to fall very rapidly and within 6-8 hours goes down to normal and even subnormal figures. The shortcoming of this method is the critical fall of the temperature which, although accompanied by a mass destruction of spirochaetes, is marked by a sharp diminution in cardiovascular functions.

It should be remembered that infusion of novarsenol at the height of an attack does not prevent recurrent attacks. The infusions must be considered more expedient on the 4th or 5th day of the first apyrexia except in cases where relapsing fever runs a severe course from its very onset and necessitates immediate administration of novarsenol to newly admitted patients.

By infusing novarsenol on the 4th or 5th day of apyrexia we avoid unpleasant and undesirable phenomena (collapse, profuse perspiration, etc.) which are accompanied by a critical fall of the temperature in cases where novarsenol is administered during the febrile attack. If novarsenol is administered during apyrexia, it suppresses the generations of spirochaetes formed after the end of the attack. To prevent recurrent attacks, the infusion of novarsenol is repeated in the same dose 6 days after the first intravenous administration. Before instituting novarsenol treatment the following contraindications must be considered: organic disease of the central nervous system, liver and kidney diseases.

Before administering novarsenol it is necessary to ascertain the period of its fitness and to record the number of its series into the case history. The preparation is fit for use only if it is light-yellow and contains no lumps. It must be infused into the vein the moment the solution has been prepared; care must be taken to infuse the preparation strictly intravenously, because penetration of novarsenol solution into subcutaneous tissue causes development of painful infiltrates. In cases of paravenous infusion hot compresses are applied to the elbow bend; this favours resorption on the infiltrates. In rare cases infusion of novarsenol may be followed by collapse due to rapid disintegration of spirochaetes in the blood; to bring the patient out of this grave condition, the patient is administered subcutaneously 0.8 ml of a 5 per cent ephedrine solution with 2 ml of a 25 per cent cordiamine solution or mesaton.

A good therapeutic effect is produced in relapsing fever by treatment with penicillin, especially at an early period of the disease. This antibiotic is administered intramuscularly in a daily dose of 900,000-1,200,000 U; the dose is divided equally into 3-4 injections or into two injections of 400,000-600,000 U each; in the latter case the preparation is diluted in a 25 per cent novocain solution. Penicillin is administered daily for 4-5 days. Small children and pregnant women should be treated only with *penicillin*. Adults are effectively treated with penicillin and novarsenol; the latter is administered twice at 6-day intervals. Administration of novarsenol is recommended during the first apyrexia.

In addition to the chemotherapeutic preparations some patients may require symptomatic agents, for example, to support the cardiovascular functions.

The patients who have developed choleraic typhoid as a complication are treated with injections of penicillin (up to 1,200,000 U per day) combined with levomycetin (0.5 g six times a day) or biomylin (300,000 U four times a day). These preparations are administered for 6-7 days, until a stable clinical effect has been produced.

All relapsing fever patients are subject to compulsory hospitalization. No patient may be discharged from the hospital before 21 days have elapsed since the end of the last attack.

An attack of the disease does not confer adequate immunity, cases of recurrent infection sometimes being observed several years later. Both cellular factors (phagocytosis of spirochaetes by leucocytes and cells of the reticuloendothelial system fixed in various organs) and humoral (formation of spirochaetolysins in the organism) are of some importance for the formation of immunity.

Prevention. Prevention of relapsing fever requires the earliest possible diagnosis of the disease, isolation of patients and carrying out of complex anti-epidemic measures in the focus of infection.

The rise in the living standards of the population and inculcation of sanitary and hygienic habits are the second most important condition for preventing the spread of this disease. An adequate network of baths, showers, delousing stations and laundries, and washing the linens with 5 per cent DDT soap help to prevent pediculosis.

If a diagnosis of relapsing fever has been established even only conjecturally, the patient is immediately hospitalized and his dwelling is subjected to a single complex all-round disinfection, including moist or gaseous (sulphur) disinsection. The clothing, linens and underwear of the patient and of the people in his surroundings are disinfected in disinsection chambers. The focus must be disinfected twice at 7-8 intervals.

In the relapsing fever focus the temperature of the people in the patient's surroundings is taken daily for 12 days in order that new cases of the disease, should there be any, may be revealed, the patient may be hospitalized and the focus may be disinfected as early

as possible. No methods of immunization against relapsing fever (preventive inoculations) have been elaborated.

Relapsing fever has been completely eradicated all over the USSR and it is therefore necessary strictly to carry out all quarantine measures to prevent the disease from being brought in from other countries.

TICK-BORNE RELAPSING FEVER (SPIROCHAETOSIS ACARINA)

Tick-borne relapsing fever is an acute general infectious disease caused by a special strain of spirochaetes and transmitted through bites of *Ornithodoros* ticks; it is characterized by recurrent attacks of fever occurring without any definite sequence. The disease occurs only in certain areas with a warm or hot climate (natural foci) under definite conditions of the vector's habitat.

Brief historical information. In Asia and Africa this disease was known in hoary antiquity. In 1913 A. N. Junkovsky, a Russian scientist, discovered the causative agent of the disease—the spirochaete of tick-borne fever—in smears of the patient's blood.

Transmission of the infection through *Ornithodoros papillipes* ticks was demonstrated by N. I. Latyshev who had let himself be bitten in the forearm by 13 infected ticks and 10 days later went down with relapsing fever.

Actiology. The causative agent of the disease is a special spirochaete (*Borrelia* *sive* *Spirochaeta sogdianum*) first described in 1913 by the Russian scientist A. N. Junkovsky.

The morphological characteristics—length and number of coils—of the spirochaete greatly vary. The number of coils averages 6-8, the spiral is 12-20 μ long and 0.3-0.35 μ thick.

To find the spirochaetes in the patient's blood, a smear or thick drop of blood stained with fuchsin is examined under the microscope. It should be remembered that there are very few of them, but, unlike louse-borne relapsing fever, the spirochaetes may be found in the patient's blood by the same method even during apyrexia (single individuals in the field of vision).

Epidemiology. The main endemic foci of tick-borne relapsing fever are in Iran and Iraq, but the disease also occurs in Afghanistan and some areas of the Soviet Central Asia republics.

The spirochaetes parasitize in the organism of ticks living only under definite climatic conditions and in the presence of appropriate biotopes, i.e., places of their habitat; the latter include walls of mud houses, gaps between the stones of fences, etc. (Fig. 43). The disease is strictly endemic. *Ornithodoros* ticks are the only reservoir of the infection, and tick-borne relapsing fever is an infectious disease with definite natural foci.

The main features of the epidemiology of this disease were elaborated by Soviet scientists (N. I. Latyshev, E. N. Pavlovsky, P. A. Petukhcheva, L. M. Isayev and others). Man becomes infected through bites of infected ticks; the infection usually takes place at night, and man therefore requires protection from the ticks during sleep.



Fig. 43. Mud-houses in Central Asia: ticks—vectors of tick-borne relapsing fever—lodge in the walls of these houses

Pathogenesis. Gaining entrance into the human organism through tick bites the spirochaetes of tick-borne relapsing fever pass in large numbers into the general circulation. This factor and their mass disintegration due to phagocytosis and the action of spirochaetolysins give rise to a febrile reaction. After the first attack some spirochaetes are retained not only in the central nervous system and in the spleen, but also in the bone marrow and the peripheral blood.

Clinical picture. The incubation period varies between 4 and 15 days (averaging 6-10 days). The disease sets in acutely: a cold fit is followed by a rise in temperature to 38.5-39.5 C.

A dark cherry-coloured papule forms on the skin at the site of the tick bite. Weakness, jadedness, slight enlargement of the spleen, icterus of the skin and moderate pain in the gastrocnemius muscles constitute the clinical picture of the first attack of the disease. The attacks are short— from several hours to 2-3 days; usually there are many attacks (6-8-12), in many cases there are 15-18 and even more. The period of apyrexia may last from 1 to 5-9 days (Fig. 44).

The febrile attacks terminate in a critical fall of the temperature and profuse sweating. Spirochaetes may be found in the blood preparations—fuchsin-stained thick drop or smear— taken during an attack; they may be found less frequently in the stained preparations of blood taken from the patient during apyrexia.

The successive attacks are separated by periods of apyrexia lasting from 2 to 8 days. The disease may last a total of 1.5-2 months.

Blood tests reveal a normal or somewhat decreased number of

leucocytes with relative lymphocytosis (up to 30-40 per cent) and monocytosis (10-12 per cent). An attack of the disease does not confer lasting immunity, and reinfection is possible.

Diagnosis. The disease is diagnosed with due consideration of the epidemiological data (sojourn in an endemic focus), anamnesis, primary affect and clinical picture. The diagnosis is confirmed by the finding of spirochaetes in a fuchsin-stained thick drop of blood.

The best results are produced by microscopy of a thick drop of the patient's blood, preliminarily dried on a slide and stained over a period of 40 minutes with the Romanovsky-Giemsa stain (2 drops of commercial stain in 1 ml of distilled water). To prepare blood preparations for spirochaete microscopy, the methods indicated in the supplement to this book are used.

Sometimes the spirochaetes are silvered by Yakimov's method, or a hanging drop of blood is microscoped under dark-field illumination (side illumination). Some use is made of negative staining of spirochaetes by Burri's method which is as follows: 1 drop of the patient's blood is mixed on a slide with 1 drop of a 5 per cent colloid silver solution or a 2 per cent Congo red solution, after which a thin smear is prepared; the microscopy is carried out by means of an immersion system, the white threads of the spirochaetes being sufficiently clearly perceived against the general smoky background.

Differential diagnosis. The disease must be differentiated from *louse-borne relapsing fever*, *malaria*, *influenza* and *pappataci fever*.

The presence of a primary affect, moderate enlargement of the spleen with no enlargement of the liver, slight muscular pains, disorderly nature of the paroxysms and monocytosis of the blood are taken into consideration; the decisive role is played by the finding of spirochaetes in a thick drop of stained blood under the microscope.

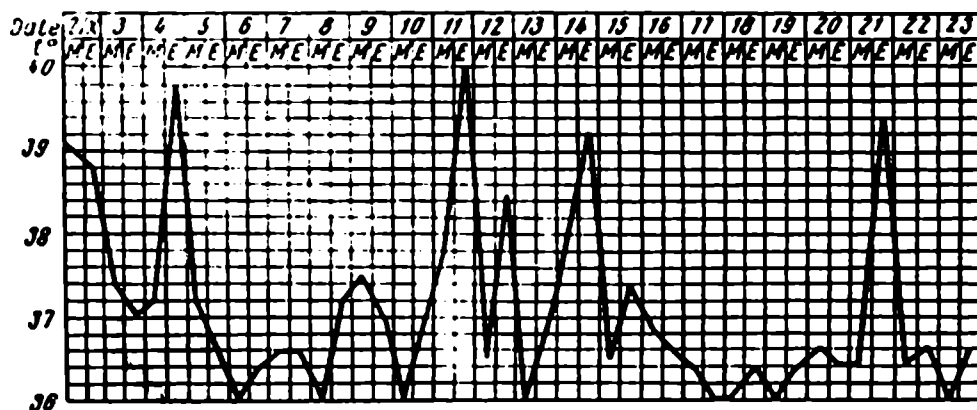


Fig. 44. Temperature curve of tick-borne relapsing fever patient

Tick-borne relapsing fever is treated with albomycin, tetracycline or biomycin.

Albomycin is administered to adults subcutaneously in a dose of 5,000,000 U twice a day; each million units of albomycin is dissolved in 2 ml of twice distilled sterile water.

Biomycin (or *tetracycline*) is administered per os in a dose of 300,000 U four times a day for 6-8 days.

Prevention. The prevention of tick-borne relapsing fever in endemic foci consists in appropriate construction of dwellings and production buildings in towns, settlements and villages (absence of cracks and gaps in the walls of dwellings and fences). DDT emulsions, chloropicrin and burning of sulphur are used in exterminating the ticks in their habitat. The legs of beds must be put in jars containing a 5 per cent DDT emulsion, which prevents the ticks from crawling into the beds from the floor. To keep infected ticks away, the skin is painted with a repellent (for example, dimethyl-phthalate).

MALARIA

Malaria is an acute infectious disease caused by malarial plasmodia (*Plasmodia malariae*—a protozoan organism), transmitted through bites of infected mosquitos (*Anopheles maculipennis*) and characterized by febrile attacks occurring at definite intervals in accordance with the cycle of development of the causative agent.

Brief historical information. Malaria is a human disease known since antiquity. Medieval treatises on medicine published in Europe and 16th-century Russian "medical aids" described diseases clinically resembling malaria.

As early as the beginning of the 18th century Lancisi (Italian) suggested a miasmatic (*mala aria*—bad air) theory of the origin of malaria, and infection with this disease was long erroneously believed to be due to swamp exhalations (hence the designation—swamp fever).

While making a histological study of the corpses of people who had died of malaria, I. Sheheglov discovered in 1871 particles of malarial pigment and suggested that its origin was a result of vital activities of pathogenic microbes. V. I. Afanasyev arrived at the same conclusion in 1879. In 1880 C. Laveran (Algeria) discovered the causative agent of malaria—plasmodium—and described its morphological characteristics.

In 1886 V. Y. Danilevsky discovered the causative agent of avian malaria, which was subsequently used as an experimental model for studying the chemotherapy of malaria.

The structure of the malarial plasmodium was thoroughly studied in the human blood by the method of double staining with eosine and methylene blue elaborated by D. L. Romanovsky in Russia in 1891. This method made it possible to distinguish the nucleus of the plasmodium from its protoplasm.

The role of *Anopheles* mosquitos (*Anopheles maculipennis*) in the transmission of malaria was demonstrated in 1898 by the English physician R. Ross who discovered the cycle of development of the plasmodia in the bodies of mosquitos. These observations were continued in Italy by Grassi who, additionally, demonstrated the possibility of infecting man with malaria experimentally.

The works published in 1948-1952 proved to be very important; a number of authors established that in addition to the forms of plasmodia developing

within erythrocytes there are also tissue forms. Owing to these investigations a number of clinical characteristics of malaria and the mechanism of action of certain antimalarial drugs were given correct elucidation. Plasmochin was synthesized in 1926; its analogue—plasmocide (pamaquine naphthoate)—was synthesized later. A number of effective medicinal preparations (acrichine [quinacrine], bigumal [paludrine] and quincide [antimalarial aminoquinoline derivative]) have been introduced into therapeutic practice since 1933.

Aetiology. Malaria may be caused by one of the four species of malarial plasmodia each of which has a number of morphological and biological characteristics. For example, *Plasmodium vivax* causes tertian malaria, *Plasmodium malariae* produces quartan malaria, *Plasmodium falciparum* brings about tropical malaria. Literature contains descriptions of several cases of a disease which resembles tertian malaria and is caused by *Plasmodium ovale*.

Tertian and tropical malaria are the most widespread. The main species of plasmodia of tertian and tropical malaria are shown in the different stages of their development in Figs. 45 and 46.

The most characteristic form of the *Plasmodium vivax* is the annular form, of the *Plasmodium malariae*—tape form, and of the *Plasmodium falciparum*—crescent form.

In the malaria patient's blood it is possible to see plasmodia located inside erythrocytes. For this purpose a thick drop of blood and blood smears stained by the Romanovsky-Giemsa method (preparation of the drop and smear is shown in Fig. 7) are examined under the microscope. Each of the four aforementioned species of plasmodia appear in their characteristic forms.

In the organism of a human malaria patient the plasmodium goes through an asexual cycle of development (schizogony), while in the body of the vector—the *Anopheles* mosquito (*Anopheles maculipennis*)—it goes through a sexual cycle of development. During the early stages of the disease, before, the developing inside erythrocytes, the plasmodia of tertian and tropical malaria are capable of developing outside of them, according to the tissue cycle which characterizes the first parasitic stages of the plasmodia in the patient's organism. The vital activities of the plasmodia reflected by the clinical picture of the disease take place mainly as the result of their parasitism and cyclic development within erythrocytes. This asexual cycle of development of the causative agent of tertian malaria is shown in Fig. 47 (forms 1-5 and 6-12). It should be remembered that in addition to schizogony, i.e., production of asexual forms of plasmodia, immature sexual forms—male (microgametocytes—13-15) and female (macrogametocytes or gametes—16-18)—are produced in the organism of a human patient; fewer sexual forms than schizonts are produced.

The asexual life cycle of plasmodia takes place in forms 1-5 (tissue stages) and 6-12 (within erythrocytes).

After sucking the blood of a human malaria patient the *Anopheles* mosquito, (B) swallows together with the blood both

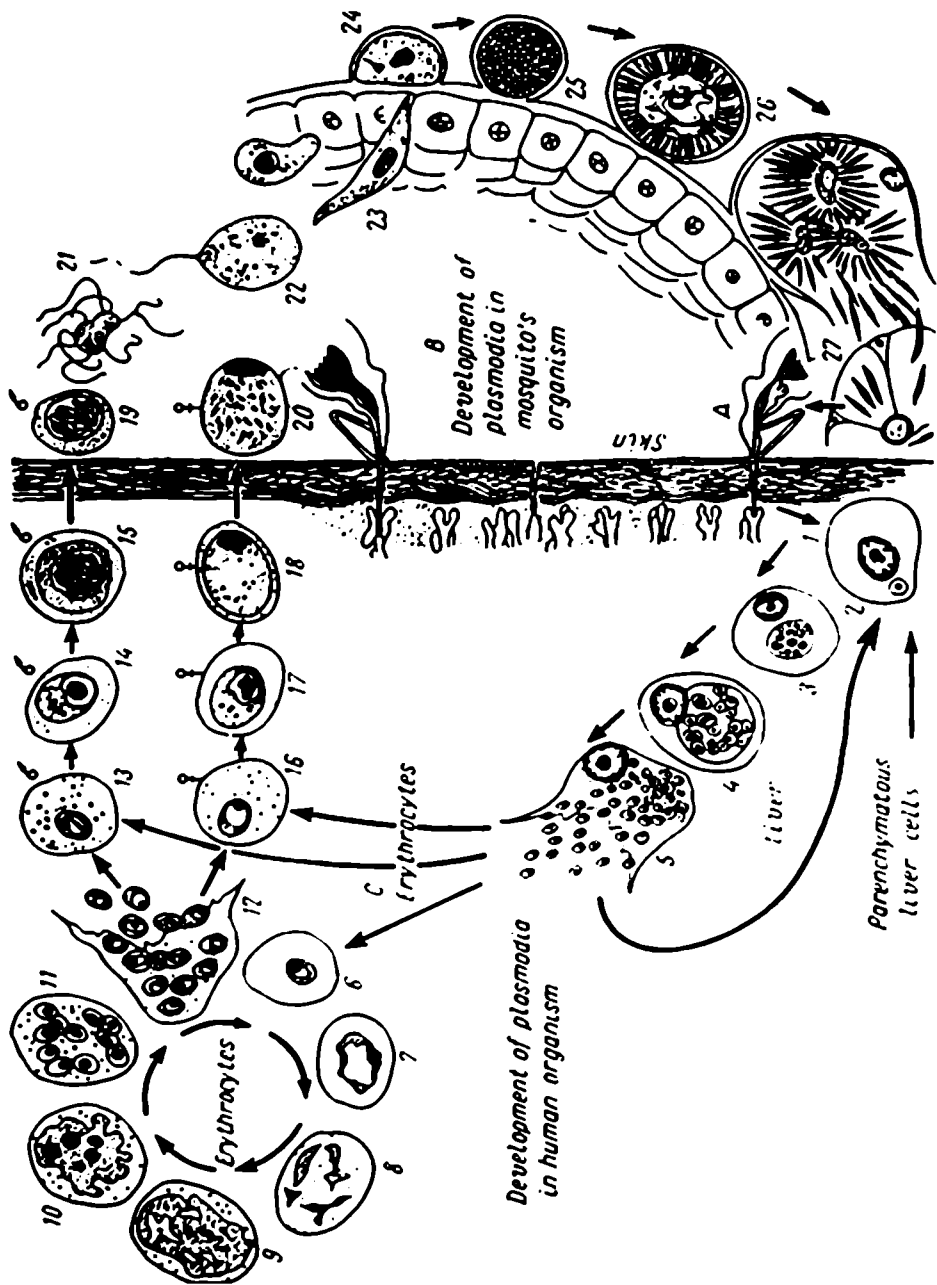


Fig. 47. Diagram showing development of a malarial plasmodium (*Plasmodium* spp.)

schizonts and sexual forms of the plasmodia—macrogametocytes and microgametocytes; the latter break up in the mosquito's stomach into filamentous forms (microgametes—21). This is followed by fertilization (22) of macrogametes by microgametes, which produces ookinetes (23); the latter penetrate into the wall of the mosquito's stomach (24) and are gradually transformed into spherical forms—oocysts (25); subsequently spindlelike forms, sporozoites (27), the youngest forms of plasmodia are produced; upon enlarging and reaching a certain degree of maturity the oocysts burst and the sporozoites are carried by the flow of haemolymph into the mosquito's salivary glands (4).

When a healthy person is bitten by an *Anopheles* mosquito infected with malarial plasmodia, numerous sporozoites are introduced together with the mosquito's saliva into the human organism (1); after going through the stage of their tissue development (2-5) the sporozoites implant themselves in erythrocytes. In the erythrocytes the plasmodia assume an annular form (6) and go through the successive stages of schizogony with formation of schizonts (6-12).

By staining the preparations of the patient's blood by the Romanovsky-Giemsa method at the stage of annular development it is possible to see clearly that inside the erythrocytes the protoplasm of plasmodia, which forms the rim of the ring, stains blue by methylene blue, whereas nucleus of the parasite stained carmine-red by azure appears as the gem of the ring.

By examining a smear of a tertian malaria patient's blood stained by the Romanovsky-Giemsa method one can see that an adult schizont (10) of a plasmodium occupies almost the entire erythrocyte which is considerably enlarged. At the same time a malarial pigment which is a product of haemoglobin transformation forms in the centre of the parasite. Subsequently the mature schizont divides into merozoites (forms 11-12). As a result of destruction of the erythrocyte the merozoites which pass into the blood flow infect other—normal—erythrocytes. This leads to a new cycle of asexual development of the plasmodia.

Some of the merozoites may serve for the production of sexual forms (macrogametocytes—16-18, and microgametocytes—13-15) with which the *Anopheles* mosquito becomes infected when sucking the patient's blood; gametes—19-20—form in the mosquito's organism. In addition to patients, carriers of sexual forms of plasmodia—gamete carriers—may also serve as sources of infection.

The cycle of development of the *Plasmodium vivax*, as most commonly also of the *Plasmodium falciparum*, lasts 48 hours, while that of the *Plasmodium malariae* lasts 72 hours. To examine under the microscope preparations of the patient's blood stained by the Romanovsky-Giemsa method, the smears and thick drop must be taken not only at the height of an attack, but also at normal temperature.

Among the plasmodia of tertian malaria it is necessary to distinguish three strains which cause malaria with different incubation periods sometimes lasting several months. For example, in the central and more northern areas of the USSR there have been cases with a very long incubation period caused by the so-called northern strain (subspecies) of plasmodium. The reasons for such long incubation have not as yet been scientifically established, but it is well-known that plasmodia are at first retained in the tissues of the human organism and cannot be found in the blood throughout the incubation period.

In 1948-1952 it was established that, in addition to the main cycle of development in the erythrocytes, the malarial plasmodia, before implanting themselves in the latter, go through certain stages of their development outside erythrocytes, namely, in connective-tissue elements of the liver and spleen (Fig. 47, tissue forms 2-5). The existence of tissue forms of the causative agents of tertian and tropical malaria has been demonstrated.

The first extraerythrocytic or tissue forms (2-5) of malarial plasmodia arise directly from sporozoites (1) which have penetrated into the human organism through the bite of the infected mosquito.

The studies of a number of investigators have shown that the tissue forms of plasmodia parasitize in connective tissue, the endothelium of blood capillaries, Kupffer's cells and hepatic cells. These tissue forms are usually divided into: (1) *pre-erythrocytic* (intermediate between sporozoites and first stages of development of plasmodia in erythrocytes) and (2) *paraerythrocytic* (existing during the period when the usual forms of development of plasmodia in erythrocytes are already present in the human organism).

Closer examination of Fig. 47 reveals that the development of asexual forms of the erythrocytic cycle (2-5 and 6-12), sexual forms (13-15 and 16-18) and tissue forms (pre-erythrocytic 2-5 and paraerythrocytic) occur in a definite succession (the arched line in the Fig. 47 shows the implantation of the causative agent in new tissue cells).

As was already noted, from the salivary glands of an *Anopheles* mosquito infected with malarial plasmodia the causative agent gains entrance into subcutaneous tissue when the mosquito bites a healthy person. In this tissue some plasmodia disintegrate, but a certain number of them may penetrate into the general circulation. The plasmodia freely circulate in the blood of the person they have invaded only about 30 minutes, after which the Kupffer's cells of the liver phagocytize the sporozoites, but some of the latter penetrate into hepatic cells where they develop as so-called *tissue forms*.

In the hepatic cells the sporozoites gradually develop into polynuclear schizonts which subsequently divide into *merozoites*; at the given stage of development they are designated as *cryptomerozoites*.

The plasmodia of tropical malaria thereby end the tissue cycle of development and after implantation of the cryptomerozoites in the erythrocytes begin their *erythrocytic cycle* of development.

The development of the causative agents of tertian malaria in tissues is more complex. Only some of the cryptomerozoites formed from polynuclear schizonts implant themselves in erythrocytes and go through the erythrocytic cycle of development. Other cryptomerozoites re enter tissue cells where they go through a second tissue cycle of development (second generation of plasmodia). Subsequently some of the tissue forms produced during the second tissue

cycle implant themselves in erythrocytes and begin a new erythrocytic cycle, while others re-enter tissue cells and immediately start the third tissue cycle.

The period of tissue development of each individual generation of malarial plasmodia in tertian malaria patients lasts 6 days and in tropical malaria patients 8 days.

Penetrating into erythrocytes the cryptomerozoites which are formed at each generation give rise to a usual erythrocytic cycle of development of plasmodia beginning with the annular form (5) and considered in detail above.

The pre-erythrocytic and paraerythrocytic forms of malarial plasmodia resist quinine and acrichine (quinacrine), and, if a short course of treatment with acrichine and quinine is administered in cases of fresh tertian malaria, remote relapses of the disease are possible.

It has been established by investigations of a number of authors that in tropical malaria merozoites do not re-enter tissue cells, and the disappearance of plasmodia from the blood, for example, in cases treated with bigumal signifies a complete clinical cure.

Epidemiology. The conditions conducive to the spread of malaria in a given area are: (a) presence of patients and gamete carriers, and (b) presence of vector mosquitos.

The females of the *Anopheles maculipennis* (the wings of this mosquito have macules, hence its designation) may be the main vector of malaria on the territory of the USSR. In addition to this vector, an important part in transmitting the disease in the southern regions of the USSR may also be played by other species of *Anopheles* mosquitos.

Owing to the closest connections between the spread of malaria and the presence of vector mosquitos this disease occurs in areas between latitude 63° North and latitude 30° South (in the eastern hemisphere).

Fresh cases of malaria appear during the period of vigorous vital activities of mosquitos, but cases of early and late relapses of the disease may also be observed outside the main season.

In the central zones of the USSR *Anopheles* mosquitos produce 2-3 generations a year.

Anopheles mosquitos live in water meadows, water reservoirs, lakes, flooded rice fields, hack-waters and swamps, and lay their eggs in water reservoirs of standing or slowly running water.

The mosquitos begin to fly out of their wintering places in the spring (in the central zone of the USSR—in April). From the second half of September they begin to settle down for the winter in cattle yards, barns, storerooms and garrets.

Development of malarial plasmodia in the mosquito's organism is possible only at a constant external temperature above 15°C. The optimum external temperature for maturation of plasmodia is 28°C; at this temperature sporogony ends in 7-8 days; at a temperature of about 17°C it ends in 35-40 days.

A mosquito that has sucked the blood of a human gamete carrier becomes contagious only after the malarial plasmodium has gone through the complete cycle of development in its organism.

Main Differences Between *Anopheles* and *Culex* Mosquitos

Stage of development	<i>Anopheles</i>	<i>Culex</i>
Eggs	Are arranged singly or as little stars on the surface of the water	Form accumulations resembling a boat on the surface of the water
Larvae	Lie parallel to the surface of the water. Have no respiratory tube (siphon). Possess palmlike hairs	Lie at an angle to the surface of the water (head down). Have a siphon
Winged mosquitoes	Most species have macules on the wings. The palpi on the female are about as long as her proboscis Sit at an angle to the surface with belly raised	Have no macules on their wings. The palpi of the female are from one-fourth to one-seventh the length of her proboscis Sit almost parallel to the surface, belly lowered

This may explain why new cases of malaria were observed in the central zone of the USSR at the end of June or in July. In this zone the highest incidence of the disease is in May and June, because of relapses, and then in August because of fresh cases and relapses with protracted incubation; in the latter cases relapses may occur 2-3 weeks after the end of the first series of attacks.

In a number of areas of the USSR located between latitude 50° North and latitude 60° North an increased incidence of the disease was observed in May and June because of cases with a long incubation period due to infection with the so-called northern strain of plasmodia at the end of summer or in autumn of the preceding year. The cases of malaria resulting from remote relapses of tertian malaria with a short incubation period were of some epidemiological importance in the northern regions of the USSR.

In the past a seasonal increase in malaria incidence was observed in the southern areas of the USSR in March in connection with relapses of tertian malaria, with a gradual increase in the incidence towards September because of fresh cases of tropical and tertian malaria.

In elucidating the circumstances of infection of man with malaria it is necessary to remember that a winged mosquito can fly 2-3 km and bite man and animals from sunup to sundown.

Clinical picture. The incubation period of tertian malaria is 9-17 days. In the northern areas of the USSR (up to latitude 60° North) the incubation period of malaria caused by so-called northern strains of plasmodia may be 5-9 months and even longer.

As a rule, malaria starts with characteristic febrile attacks (paroxysms). A constant type fever lasting 6-8 days may be observed only in some fresh cases of malaria, periodic paroxysms following afterwards. A description of the clinical picture of tertian malaria with attacks recurring every 48 hours is given below. The febrile attack of a malaria patient may occur at any time of the day, but usually occurs at about 11 o'clock in the morning. The attack begins with chilliness or intense chills. The patient cannot get warm, and this makes him wrap himself up and pull the blanket over his head. The chills are followed by a rapid elevation of temperature to 40-41°C and even higher; the patient develops a headache, tachycardia, sometimes nausea, and even begins to vomit. At the height of the attack, when the temperature is very high, the patient throws off his blanket; he is very hot and is tormented by thirst. At this time his skin is dry and very hot to touch, the face is red and the lips are dry; a herpetic eruption is often observed on the mucosa of the lips.

About 5-6 hours after the beginning of the attack the patient begins to sweat copiously so that it is necessary to change his underwear and bed linens. Then the temperature falls critically to normal or even subnormal figures, but the patient continues to sweat profusely. At this time the patient is considerably relieved, although still very weak. Often the patient falls asleep after the drop in temperature and resting up during his long sleep (10-12 hours) feels quite satisfactory.

The interval between the end of one febrile attack and the beginning of another is called the period of *apyrexia*.

One of the important differences between the various forms of malaria is the periodicity of the febrile attacks.

In tertian malaria 48 hours elapse *from the end of one attack to the beginning of the next*. In quartan malaria this interval is 72 hours. The attacks of tertian malaria are characterized by strict periodicity, i.e., they begin at the same time of the day, although in some cases they may be 2-3 hours early or late. The attacks of tropical fever are not strictly periodic, the febrile period is prolonged, the temperature curve is very irregular, and the temperature often rises again soon after its fall.

In some cases of tertian malaria the attacks occur without their characteristic phenomena, i.e., the period of pyrexia may be prolonged and there may be no difference between the morning and evening temperature. Owing to this it is necessary, at the slightest suspicion of malaria, to measure the patient's temperature every 2 hours for 3-4 days.

If the patient is infected with two different generations of malarial plasmodia, the attacks occur more often at intervals of several hours; in such cases, as in cases of inadequate treatment, the disease may run a protracted course.

The pathogenesis of malarial attacks is not yet sufficiently clear. It may be considered with certainty only that the disturbed balance between heat production and heat loss in the patient's organism, owing to which chills appear and the temperature rises, is due to the action of foreign proteins of the plasmodial protoplasm and the malarial pigment which pass into the blood plasma from the erythrocytes during the break-up of an adult schizont into individual merozoites. The appearance of chills corresponds to the moment the merozoites pass from the erythrocytes into the blood flow. Immune factors lead to mass destruction of plasmodia. The dependence of the temperature curve on the main cycle of development of the plasmodia in various forms of malaria is shown in Fig. 48.

With the progress of malaria organs and systems exhibit a number of pathologic changes which are especially clearly marked in cases of insufficiently vigorous treatment. Very soon after the onset of the disease the liver and spleen begin to enlarge; in protracted cases these organs become considerably enlarged.

A mild icterus of the sclerae and skin appears as early as the tenth or twelfth day of the disease; this is due to haemolysis of erythrocytes and affection of the parenchyma of the liver.

In fresh cases of malaria vesicular (herpetic) eruptions often appear on the skin of the face, around the nose and on the upper or lower lip.

The height of an attack is characterized by tachycardia, the borders of the heart are slightly extended to the left, and somewhat dull apical heart sounds are auscultated. In protracted cases of either entirely untreated or inadequately treated malaria auscultation of the heart sometimes reveals a mild systolic murmur which is due to anaemia. Some protracted cases of malaria may be accompanied by oedema of the feet, shanks and the lumbosacral region. The blood picture begins to show a number of characteristic changes as early as the 6th or 8th day of the disease. Progressive hypochromic anaemia, thrombocytopenia, marked leucopenia with neutropenia, relative lymphocytosis and monocytosis, a shift of the neutrophilic group of leucocytes to the left and a considerably accelerated ESR are noted towards the 12th day of the disease. This blood picture is characteristic mainly of the period of apyrexia, while attacks may be characterized by moderate leucocytosis which develops as a result of the increase in the number of neutrophilic leucocytes.

As a rule, malaria patients have a poor appetite; the attacks are accompanied by pressure in the epigastrium and nausea. In some cases there may be diarrhoea. In protracted cases of the disease the abdomen is enlarged because of the enlarged liver and spleen.

As the result of proliferation of reticuloendothelial elements, deposition of malarial pigment (melanin) and certain growth of connective tissue, the liver and spleen in protracted cases appear compact to touch. Development of chronic malarial hepatitis and

cirrhosis of the liver is possible; the signs of these affections are a sallow complexion, a continued enlargement of the liver and its considerable compactness.

The symptoms of disturbances in the nervous system of persons long affected with malaria are headaches, irritability and rapid fatigability.

The foregoing was a description of the clinical course of tertian malaria.

Tropical malaria occurs predominantly in severe forms; comatose and fulminant forms of the disease are observed more often than in cases of tertian malaria.

Complications. Any form of malaria, particularly tropical malaria, may be accompanied by complications.

The usual course of malaria is sometimes aggravated by a severe depression of the central nervous system manifested in *malarial coma*. This is fostered by sensitization and intoxication of the organism by the products of disintegration of malarial plasmodia and disorganization of the blood circulation in the brain as a result of obstruction of the cerebral capillaries by an enormous number of plasmodia. The onset of coma is often preceded by a period of considerable sleepiness—precomatose state. Coma may set in at once or may develop over a period of 2-3 hours. Although malarial coma constitutes a great danger, timely and vigorous therapeutic measures make it possible to bring the patient out of this extremely grave condition.

A neurological examination of a patient in a comatose state reveals that the tendon reflexes (patellar, Achilles, etc.) are at first intensified, but with the progress of coma diminish or disappear. Usually meningeal phenomena are strongly pronounced, tonic spasms and hypertonia of flexor muscles are observed, and trismus is possible. The expression of the patient's face is indifferent, the skin is dry, yellowish and sallow, the pupils are dilated, the sclerae are icteric. The pulse is sharply accelerated, small and feeble, sometimes even thready; the blood pressure is lowered. Respiration is accelerated, its rhythm is often disturbed, and it resembles Cheyne-Stokes respiration. Deglutition is impaired, the abdomen is inflated, the liver and spleen are enlarged, and the stool is usually retained. The temperature is for the most part elevated (40-41°C). A test of the morphological composition of the blood reveals leucocytosis with a shift to the left; the blood preparations stained by the Romanovsky-Giemsa method show a large number of malarial plasmodia.

Of the complications of malaria special mention must be made of nephrosonephritis, malarial hepatitis and haemoglobinuric fever.

Acute diffuse nephrosonephritis in malaria patients is characterized by appearance of oedemas and presence of erythrocytes and protein in the urine; only some patients have arterial hypertension.

As a rule, the affections of the kidneys in malaria are eliminated by bed rest, antimalarial therapy (acrichine, bigumal), a dairy and vegetable diet and limited drinking.

The symptoms of acute malarial hepatitis are icterus of the skin and sclerae, considerable enlargement and painfulness of the liver, increasing bilirubinaemia (with a direct van den Bergh reaction) and distortion of functional liver tests.

Haemoglobinuric fever is a comparatively rare complication of malaria observed during intervals between the attacks mainly in severe forms of the disease and most commonly in patients treated with quinine.

The signs of this complication are progressive anaemia, icterus of the skin and sclerae of haemolytic origin (indirect reaction to the blood bilirubin), enlargement of the liver and spleen, persistent haemoglobinuria with haemoglobin and products of its transformation, for example methaemoglobin, eliminated in the urine. Fulminant forms of haemoglobinuric fever may lead to lethal results.

A special category of clinical symptoms of malaria consists of the pathologic conditions which are most intimately connected with the pathogenesis of malaria and may accompany uncomplicated febrile attacks or develop some time after their cessation, namely, metamalarial and paramalarial diseases. They include severe forms of anaemia, stable splenomegaly and cirrhosis of the spleen, malarial melanosis and cirrhosis of the liver, encephalopathy with mental disturbances.

Malaria may have *relapses* which are characterized by the same febrile attacks as the primary disease.

There are *early relapses*—within 6-8 weeks, and *late relapses*—5-9 and more months after the end of the first wave of attacks.

Early relapses occur mainly in cases of inadequate treatment; late relapses are due to general cooling of the organism, ultraviolet irradiation in the spring, physical overwork or nervous shock.

In the central and northern areas of the European part of the USSR late relapses were noted in May or the first half of June. Malaria is classified, according to its clinical course, as follows.

1. Primary disease and early relapses.
2. Late relapses and recurrent diseases.
3. Paramalarial diseases.
4. Carrying of malarial plasmodia.

The clinical course of malaria in primary cases and relapses must be divided into mild, moderately severe and severe, taking into consideration the duration of the disease, the febrile attacks and their frequency.

After a single infection with plasmodia man may have the disease for 1.5-2 years; the existence of chronic malaria is now denied. It should be remembered, however, that in areas where there is malaria

incidence man is in danger of reinfection and, consequently, of recurrent malaria. This is due to the inadequate immunity conferred by the primary disease.

Pathologic anatomy. Examination of the parenchymatous organs of people who have died of malaria reveals a deposit of malarial pigment in the liver, spleen, lymph nodes and bone marrow; characteristic of the liver and spleen is their slate colouring because the reticuloendothelial elements have seized particles of the malarial pigment. A protracted course of malaria leads to melanosis of the liver. The spleen is enlarged, compact and not infrequently has necrotic foci. Histological examination shows hyperplasia and sclerosis of the pulp and numerous deposits of haemomelanin and haemosiderin.

Histological examination of the brain of people who have died of malarial coma reveals a large number of plasmodia obstructing the lumens of blood capillaries, stasis and minute haemorrhages into the cerebral substance. The white matter of the brain exhibits nodular growth of the glia cells in the form of rosettes.

Prognosis. With timely diagnosis and vigorous treatment all cases of malaria end in recovery. In severe forms of malaria, especially tropical malaria, the prognosis is serious. The development of complications considerably aggravates the prognosis, particularly dangerous to patients is malarial coma.

Diagnosis. To diagnose malaria, the data of epidemiology and anamnesis and the clinical picture of the disease, described in detail above, are used; discovery under the microscope of malarial plasmodia in the patient's blood preparations (smear and thick drop) stained by the Romanovsky-Giemsa method serves as an authentic confirmation of the diagnosis.

It should be emphasized that the probability of finding plasmodia in the thick drop is much greater than in the smear since the thick drop contains more blood than the smear, while the presence of haemolysed and unstained erythrocytes in the thick drop does not prevent good staining of the plasmodia.

The drop of the patient's blood obtained by a puncture made with a special needle is put on a clean dry slide and is carefully spread till it forms a spot 1 cm in diameter. The thick drop thus prepared is dried in the air and Romanovsky-Giemsa's diluted stain is poured on the preparation (1 drop of stain per 1 ml of distilled water). The erythrocytes are thereby haemolysed. The thick drop is stained over a period of 40 minutes, then the preparation is carefully rinsed with tap water, and the slides with the preparation stood up vertically are dried in the air at room temperature. To test the blood for malaria, the thick drop may be taken not only during attacks, but also outside of attacks, even at perfectly normal temperature.

Whereas during the first days of the disease with a constant type fever curve it is sometimes difficult to establish a diagnosis, the appearance of characteristic malarial attacks considerably facilitates the diagnosis.

During the first 6-8 days of fresh cases of malaria (especially tropical), when the temperature persists on constantly high figures, it may be necessary to differentiate the disease from typhoid fever, brucellosis, miliary tuberculosis, pneumonia, relapsing fever and sepsis of various aetiology.

Taking into account the presence or absence of clinical symptoms of the diseases enumerated above and the data of corresponding laboratory tests it is necessary to consider in differential diagnosis such sufficiently characteristic signs of malaria as icterus of the skin and sclerae, tachycardia, early enlargement of the liver and spleen, leucopenia and relative lymphocytosis. Discovery of malarial plasmodia in a blood smear stained by the Romanovsky-Giemsa method helps to establish a final diagnosis of malaria. It is advisable to take several blood preparations in the course of the day, and to measure the temperature every two hours in order to reveal effaced attacks of the disease.

In cases of coma malaria must be differentiated from epidemic cerebrospinal meningitis and from hepatic, uraemic and diabetic coma; to settle the question of the diagnosis, it is extremely important to make a repeated microscopic examination of a smear and thick drop of blood stained by the Romanovsky-Giemsa method.

In addition to the clinical picture, the diagnosis of malarial coma is confirmed by discovery of malarial plasmodia in the patient's blood.

Treatment. For the treatment of fresh cases of malaria, as well as its early and late relapses, all patients should be hospitalized in order that the first attacks of the disease may be cut short. During repeated therapeutic courses at the time of apyrexia and antirelapse treatment malaria patients may be treated out of hospitals.

During the first days of fresh cases of malaria and during attacks patients are given easily assimilable, semiliquid and high-calory, vitamin-rich food.

Protracted malaria often leads to marked anaemia. In such cases patients are prescribed preparations of iron and brewer's yeast, and are given blood transfusions in divided portions (150-200 ml every other day). This is particularly necessary in severe forms of the disease accompanied by considerable depression of the haematopoietic functions.

The most important chemotherapeutic agents for malaria patients are quinine, plasmocide, acrichine, bigumal and quinocide. The last three antimalarial preparations are particularly frequently used for they have completely replaced quinine.

A 50 per cent solution of quinine dihydrochloride is administered intramuscularly in a dose of 1 ml 3 times a day only in malarial coma.

Acrichine acts mainly on schizonts and produces no appreciable effect on gametocytes and tissue forms of malarial plasmodia.

The preparation is dispensed in the form of a yellow fine-crystal powder or yellow pills (acrichine hydrochloride). It may be administered intramuscularly in the form of a 4 per cent solution in a dose of 7-8 ml per injection twice a day for 3 days. During the injection the acrichine solution must not be allowed to get into subcutaneous tissue where it may produce necroses. The acrichine solution is sterilized by boiling. If crystals of acrichine have settled to the bottom of vial, the solution must be heated to 40 C and then cooled to room temperature before it is administered to the patient intramuscularly. The therapeutic dose of acrichine is 0.1 g, but in the treatment of malaria during the first cycle, shock doses of 0.2 g and even 0.3 g are often used. Acrichine is administered in 3 short therapeutic courses at 7-day intervals.

Administration of acrichine for a long time makes the skin (but not the sclerae!) yellowish because of accumulation of acrichine in the patient's organism.

As a rule, acrichine produces no side effects, but neuropsychic disturbances to the point of acute acrichine psychoses are possible in cases where acrichine has been considerably overdosed. The changes in the patient's mental reactions (acrichine intoxication, euphoria), which, although rarely observed, are the result of the toxic action of the drug, serve as an absolute indication for discontinuance of acrichine treatment.

Acrichine is contraindicated for patients with marked liver affection and uraemia.

The group of gametocidal drugs, effective mainly against gametocytes and to a lesser extent against schizonts, includes *plasmocide*; this drug is apparently also effective against tissue forms of plasmodia.

Plasmocide is a yellow-orange-coloured, slightly bitter powder insoluble in water. Its average single therapeutic dose for adults must not exceed 0.02 g. Plasmocide overdosing is accompanied by pains in the epigastrium and paraesthesias and pains along the course of the trigeminal nerve. In such cases administration of the drug is immediately suspended, the stomach is washed out, a glucose and physiologic solutions are infused intravenously and subcutaneously respectively, and cardiovascular agents are administered. Severe plasmocide poisoning may result in atrophy of the optic nerve and total blindness.

Plasmocide treatment is contraindicated in cases of diseases of the retina and the optic nerve, and organic affections of the central nervous system.

A good therapeutic effect and a decrease in the frequency of relapses of malaria are produced by combining plasmocide with acrichine.

Plasmocide is dispensed together with acrichine in bright-green pills (stained with methylene blue). Owing to the stain it is easy

to distinguish the pills containing plasmocide and acrichine from those containing only acrichine. The pills for adults contain 0.1 g of acrichine and 0.02 g of plasmocide.

The following is a scheme for treating malaria with acrichine and plasmocide.

Scheme of a Course of Treatment with Acrichine and Plasmocide

Cycles and intervals	Duration	Acrichino	Plasmocide	Note
		Single dose in grams		
First cycle 4 days	First day	0.2	0.02	The drugs are given in the indicated doses three times per day
	Second day	0.1	0.02	
	Third day	0.1	0.02	
	Fourth day	0.1	0.02	
Interval	Seven days			
Second cycle	Three days	0.1	0.02	
Interval	Seven days			
Third cycle	Three days	0.1	0.02	

Bigumal, a synthetic antimalarial preparation, was recently introduced into therapeutic practice. It is a white, bitter crystalline powder readily soluble in water and is administered in the form of bigumal acetate and bigumal hydrochloride.

A single dose of bigumal is 0.1 g, but the drug is scarcely toxic and the single dose may therefore be increased to 0.3 g.

Bigumal is the most effective in the treatment of tropical malaria; the plasmodia of tropical malaria disappear as early as the third day of treatment. Bigumal produces a marked schizontocidal effect; relapses of tropical malaria are observed in no more than 10 per cent of the cases treated with this drug. In tropical malaria it also suppresses the tissue development of plasmodia.

Below is a scheme for treating malaria with bigumal. A complete therapeutic course requires 1.8 g of the drug.

Scheme of a Course of Treatment with Bigumal

Day of the course	Daily dose in grams	Note
First	0.6	Two intakes at 6-hour intervals
Second	0.3	
Third	0.3	
Fourth	0.3	
Fifth	0.3	One intake

As a rule, bigumal is well tolerated by all patients; only rarely are nausea, headache, and neutrophilic myelocytes in the blood observed. Of the other aspects of the chemotherapeutic action of bigumal mention must be made of its gametostatic effect on malarial parasites in the body of the mosquito (it shows an ability to suppress the development of plasmodia in the vector's organism); this is utilized for chemoprophylaxis of malaria.

To produce the fastest and completest therapeutic effect and to eliminate gamete-carrying, at the same time reducing the number of relapses to the minimum, a scheme of a 7-day treatment with acrichine, plasmocide and bigumal has been elaborated; this scheme is widely used in the Soviet Union.

Scheme of 7-day Treatment of Malaria with Acrichine, Plasmocide and Bigumal (APB Scheme)

Day of the course	First intake			Second intake			Note
	Acry- chine	Plas- moicide	Bigu- mal	Acry- chine	Plas- moicide	Bigu- mal	
	in grams						
First	0.2	0.02	0.2	0.1	0.02	0.1	1 All three drugs are taken simul- taneously
Second	0.2	0.02	0.2	0.1	0.02	0.1	
Third	0.2	0.02	0.2	0.1	0.02	0.1	
Fourth	0.2	0.02	0.2	0.1	0.02	0.1	2 The interval be- tween the first and second intakes is 6-8 hours
Fifth	0.2	0.02	0.2	0.1	0.02	0.1	
Sixth	0.2	0.02	0.2	0.1	0.02	0.1	
Seventh	0.2	0.02	0.2	0.1	0.02	0.1	

Hospital patients need very careful watching because plasmocide may produce side effects; the harmful influence of the drug on people particularly sensitive to it must be stopped in due time.

To prevent malaria relapses, *antirelapse* treatment is administered; this treatment is instituted 1.5-2 months after the end of the main course.

Any of the above schemes may be used for antirelapse treatment, but the daily doses of the drugs are reduced by one-third. The antirelapse treatment is repeated the following year— in the beginning of April in cases of tertian malaria and in August-September in cases of tropical malaria.

The treatment of patients in a state of malarial coma is fraught with considerable difficulties.

Such cases require vigorous antimalarial treatment, namely, 8 ml of a 4 per cent acrichine solution 2-3 times per day intramuscularly, 0.5 g of quinine hydrochloride twice a day intramuscularly, preparations stimulating blood circulation and respiration

(ephedrine, camphor, lobeline, cytitone) and simultaneous subcutaneous and intravenous infusions of a 5 per cent glucose solution and physiologic solution. The period for which it is necessary to administer antimalarial drugs in coma is determined by the resultant therapeutic effect.

In cases of complications (nephritides, hepatitides) and parmalarial conditions (anaemia) treatment is administered according to general therapeutic rules simultaneously with antimalarial treatment (mainly with bigumal).

Of late the following new drugs are being used in the treatment of malaria: *quinocide*, *chloroquine* and *amodiaquin*; *quinocide* is effective against the tissue forms of plasmodia of tertian malaria. The course of treatment begins with peroral administration of acrichine (0.1 g 3 times per day) and plasmocide (0.02 g 3 times per day) for 7 days. This course is followed by a 10-day interval after which *quinocide* is administered (0.01 g twice a day for 15 days in succession). When treated according to this scheme, 96-98 per cent of all patients with fresh malaria are completely cured.

Treatment of all forms of malaria with *chloroquine* is administered for three days running.

Chloroquine is given per os in a dose of 0.6 g on the first day (in 2 intakes) and 0.3 g (1 intake) on the second and third days.

Amodiaquin is administered 3 days in succession in a dose of 0.6 g on the first day and 0.4 g on the second and third days.

Prevention. The measures of malaria control consist in extermination of the vectors of the disease—*Anopheles* mosquitos, systematic revealment of malaria patients, rational treatment and administration of courses of antirelapse treatment.

To exterminate the vectors of malaria, hydrotechnical and hydro-meliorative work is carried out (swampy areas are dried and water reservoirs are cleaned), the larvae of the *Anopheles* mosquito are destroyed on the surface of closed water reservoirs (lakes, swamps and ponds) by petrolization and spraying of Paris green emulsion.

The experience of malaria control in the USSR has shown overall dusting of the breeding places and habitat of mosquitos with stable insecticides—DDT and hexachlorocyclohexane—to be very effective. Dusting or spraying the walls, ceilings and windows of dwellings and production building with powders or emulsions containing stable insecticides (DDT or hexachlorocyclohexane) is a reliable method of exterminating winged *Anopheles* mosquitos.

In addition to the aforementioned measures man needs mechanical protection from the bites of mosquitos. For such protection the windows of buildings and the entrance doors are screened with a fine metal meshwork and a gauze canopy is made over the bed. In a wood or field it is best to sleep under a mosquito net.

Zooprophylaxis of malaria is also of some significance; if pastures and cattle-yards are located between dwellings and mosquito breed-

ing places, the cattle attracts the *Anopheles* mosquitos thereby helping to protect man against attacks of these vectors of malaria. Radical treatment with quinocide successfully solves the problem of rational prevention of malaria.

Timely revealment of malaria patients and their rational treatment are important measures of preventing the spread of the disease. Systematic treatment, including antirelapse treatment, leads to liquidation of gamete-carrying. It is necessary to examine under the microscope smears and thick drops of blood (stained by the Romanovsky-Giemsa method) of every patient suspected of malaria, especially during spring and summer and wherever malaria occurs.

In addition to the above measures, *chemoprophylaxis* of malaria is used. The following drugs are recommended: bigumal (0.1 g twice a week) or acrichine pills (0.1 g) with plasmocide (0.02 g) in a dose of 1 pill twice a day for 2 days, repeating the two-day course at intervals of 5 days.

In the central geographical zone of the USSR chemoprophylaxis was conducted according to this scheme from April to October wherever there were cases of malaria.

The success of chemoprophylaxis of malaria is based on extermination of sporozoites and pre-erythrocytic tissue forms of malarial plasmodia by drugs.

Malaria has been eradicated in the USSR, primarily in the central geographical zone, by careful revealment and rational treatment of patients and gamete carriers, extermination of the vector at all stages of its development, and chemoprophylaxis. The success in the control of malaria was favoured by systematic overall anti-epidemic measures.

CUTANEOUS LEISHMANIASIS (LEISHMANIOSIS CUTIS)

Cutaneous leishmaniasis (oriental or Tashkend sore) is a general infections disease caused by a protozoan parasite (*Leishmania tropica*); it is transmitted through bites of sandflies. It occurs in some countries with a hot climate and is characterized by ulceration of the skin.

Brief historical information. Leishmaniasis has been described under various local designations in a number of countries with a hot climate (Asia, Africa and some areas in Southern Europe).

The causative agent (*Leishmania tropica*) was discovered in granulations of the oriental sore by the Russian scientist P. F. Borovsky in 1898. In Russia an important contribution to the theory of leishmaniasis was made by V. L. Yakimov, Y. I. Martsinovskiy, N. I. Latyshev and others.

Aetiology. The causative agent of the disease (*Leishmania tropica*) belongs to the family of trypanosomes (class of flagellates). The causative agents of cutaneous and visceral leishmaniasis are morphologically very similar.

The biological peculiarity of the causative agent of cutaneous

leishmaniasis is that it parasitizes intracellularly. Leishmaniae can be cultivated in the NNN medium, so designated by the first letters of the names of three authors (Nicolle, Novy and MacNeal); it consists of agar with an addition of rabbit blood.

Epidemiology. Rodents—inhabitants of deserts (particularly gophers and gerbils)—and apparently dogs are the main reservoir of the infection in nature, the former transmitting “early ulcerating” cutaneous leishmaniasis and the latter fostering the spread of “late ulcerating” leishmaniasis. A certain part in the epidemiology of leishmaniasis is played by patients.

The vectors of cutaneous leishmaniasis are two different species of sandflies—*Phlebotomus pappatasi* (see Fig. 53) and *Phlebotomus sergenti*. After sucking the blood of an infected rodent the sandflies become an intermediate reservoir of the infection.

The “late ulcerating” forms of leishmaniasis are transmitted from patients to healthy people by the same species of sandflies.

Owing to a number of biological characteristics of the vector sandflies, and in cases of “early ulcerating” cutaneous leishmaniasis also as a result of a number of specific conditions of habitat of wild rodents as reservoirs of the infection, the spread of the disease is strictly focal, i.e., the disease has *natural foci*.

Cutaneous leishmaniasis occurs mainly in Egypt, Tunisia, Abyssinia, Asia Minor, Iran, Iraq and Afghanistan; cases of this disease have also been observed in various areas of Central Asia.

Cutaneous leishmaniasis is characterized by seasonal occurrence. It occurs mainly in autumn because autumn is the time of the most vigorous activities of sandflies.

An attack of the disease confers lasting immunity.

Pathogenesis. Through the bite of a sandfly leishmaniae gain entrance into the human skin where they parasitize intracellularly, mainly in connective-tissue elements. The vital activities of the leishmaniae disturb tissue nutrition and give rise to necroses with formation of ulcers.

Clinical picture. On the basis of the clinical course of the disease the latter is divided into “early ulcerating” and “late ulcerating” cutaneous leishmaniases.

The incubation period of “early ulcerating” leishmaniasis lasts from several days to 1.5 months, while that of the “late ulcerating” form lasts from 2 to 6 months.

One of the first clinical manifestations of “early ulcerating” leishmaniasis is a bright-red nodule about 1 cm in diameter surrounded by a zone of perifocal oedema at the atrium of infection on the skin.

Within 2-3 weeks necrosis with a typical scab develops in the centre of this area; when the scab falls off it leaves an ulcer with dentate edges and a red floor. Then new nodules appear around the ulcer and go through the same successive development. During



Fig. 49. Cutaneous leishmaniasis. Ulcers on the forearm and hand (from E. N. Pavlovsky)

the immediately following 4-5 months the ulcer enlarges and may reach 10-15 cm in diameter; its copious sero-purulent discharge dries on the surface in the form of a large dirty-grey or brown crust. After epithelization a small scar remains at the site of the ulcer.

In "late ulcerating" (or "dry") leishmaniasis a small infiltrate of up to 3 mm in diameter forms on the skin first; the centre of the infiltrate has an indentation in the form of a crater covered with minute scales. Then the affected area of the skin becomes covered with a crust and an ulcer up to 3 mm deep develops directly under the crust. Several months later the ulcer begins to cicatrize, the cicatrization taking one year or even longer.

In cutaneous leishmaniasis ulcers form mainly on exposed parts of the body (face, ears, hands, shank and foot) because that is where sandflies bite (Fig. 49).

Sometimes there are simultaneously several ulcers on different parts of the skin.

Of the clinical varieties of cutaneous leishmaniasis special mention must be made of serpiginous (creeping) forms of the disease which are characterized by a "creeping" spread of the pathologic process; abundant papillomatous growths are also observed. Some patients develop lymphangitis and regional lymphadenitides connected with the region of the cutaneous ulcer.

An attack of cutaneous leishmaniasis confers lasting immunity.

Diagnosis. In diagnosing cutaneous leishmaniasis it is necessary to be guided by epidemiological data and the clinical picture. If a person living in an area where there are cases of cutaneous leishmaniasis develops a papule on the skin, the papule ulcerates and the ulcer discharges sero-purulent matter (in cases of the "early ulcerating" form—Fig. 50), or the person develops a primary deep ulcerous defect of the skin (in the "late ulcerating" form) with

subsequent formation of a crust and growth of granulations, a diagnosis of cutaneous leishmaniasis may be established with certainty. It is desirable, however, to confirm the diagnosis by a laboratory test, for which purpose pieces of granulations are taken with a cotton tampon from the floor of the ulcer cleansed from pus, a smear is made on a slide and stained by the Romanovsky-Giemsa method. If the diagnosis is correct, microscopy will reveal leishmaniae.

Prognosis. Although cutaneous leishmaniasis is a protracted disease, it usually ends in recovery. The scars it leaves sometimes produce cosmetic defects - contraction of the lids, deformation of the pinna of the ears, etc., and disturbances in various functions, for example, impairment of nasal breathing in cases of deformation of the nose and nasal passages.

Treatment. No effective specific agents have been elaborated. Early ulcerating cutaneous leishmaniasis is treated with sulphonamides (norsulphazol [sulphathiazole] in a dose of 0.5 g 6 times per day for 7-8 days). Wet cutaneous ulcers are dusted with norsulphazol powder. Patients are recommended additionally to take biconycin per os (200,000 U 4 times per day).



Fig. 50. Cutaneous leishmaniasis with ulcers localized on the face

In the treatment of patients suffering from "late ulcerating" leishmaniasis disinfecting ointments [1 per cent rivanol (2-ethoxy-6,9-diaminoacridine lactate) ointment and 1 per cent acrichine ointment] are applied to the ulcers and the nodules are impregnated with a 5 per cent acrichine solution at an early stage of their development. To increase the reactivity of the organism, general roborant treatment (blood transfusions, haemotherapy, adequate high-calory diet, vitamins) is recommended.

Prevention. The most important part in preventing cutaneous leishmaniasis is played by extermination of the vectors of the infection—sandflies—at their breeding grounds, for example, by dusting the burrows of rodents, windows, etc., with a 10 per cent DDT powder. To prevent the spread of the infection, patients with ulcers on exposed parts of the body must wear aseptic bandages. To protect people from sandflies, the doors and windows of dwellings and production buildings must be provided with fine mesh screens and the beds with gauze mosquito nets.

Wild rodents (gophers and gerbils) which are the main reservoir of the infection in nature are exterminated with chloropicrin and other methods of deratization. Inoculations with a leishmania culture have been suggested.

VISCERAL (GENERAL) LEISHMANIASIS (LEISHMANIASIS INTERNA. KALA-AZAR)

Visceral leishmaniasis is a general infectious disease caused by a special species of protozoans (*Leishmania donovani*) and transmitted by sandflies (vectors of the infection); the disease is characterized by a protracted course, remittent fever, general cachexia, progressive anaemia and extreme enlargement of the spleen.

Brief historical information. In Mesopotamia, Asia Minor and Mediterranean countries the disease was known in hoary antiquity. In Central Asia it has long been known as kala-azar.

P. F. Borovsky discovered the causative agent of cutaneous leishmaniasis in 1898; in 1904 two English physicians—Leishman and Donovan—almost simultaneously, but independently of each other, described the causative agent of *visceral leishmaniasis*, which was subsequently named *Leishmania donovani*, after Leishman and Donovan.

Soviet scientists—V. L. Yakimov, Y. I. Martsinovsky, E. N. Pavlovsky, N. I. Latyshev, A. N. Khodukin and others—have made a very important contribution to the study of leishmaniasis and the elaboration of methods of controlling this disease. A. N. Khodukin, for example, has established the connection of this disease in man with leishmaniasis in dogs.

Aetiology. The causative agents of various forms of leishmaniasis are very similar morphologically. They belong to the family of trypanosomes, class of flagellates.

The *lanceolate* form of this parasite (*Leishmania donovani*) is 18-20 μ long (without the flagellum); it lives in the digestive tract

of its main host—the sandfly. While parasitizing in the organism of its second host—vertebrate animals or man—the leishmaniae undergo considerable morphological changes and become ovoid or round nonmotile structures 2-4 μ long; they are usually located intracellularly, mainly in macrophages, i.e., connective-tissue cells.

By staining histological preparations containing leishmaniae by the Romanovsky-Giemsa method it is possible clearly to see under the microscope that the body of a leishmania has a rather large violet-red nucleus surrounded by blue protoplasm; it is also possible to see a blepharoblast—rod-shaped body of the parasite from which a thin flagellum grows (flagellated form).

In the special NNN nutrient medium consisting of agar and rabbit blood leishmaniae produce a flagellated form. To isolate a pure culture, an inoculation is made in condensation water of sterile test-tubes containing the NNN medium. Small round colonies appear on the surface of the agar after 2 days of growth at 22-23°C.

In the body of the sandfly leishmaniae assume the form of a cigar.

Epidemiology. Mesopotamia, Mediterranean countries, India and China are the main endemic foci of visceral leishmaniasis. Cases of this disease are also observed in Central Asia where the disease usually attacks children.

Under natural conditions leishmaniasis affects dogs who are a reservoir (carriers) of the infection. Dogs affected with visceral leishmaniasis have blepharitis and conjunctivitis, ulcers of the skin, especially in the region of the pinna of the ear; in severe cases such animals die.

By sucking the blood of an infected dog the sandflies (*Phlebotomus chinensis*, *Phlebotomus sergenti*, *Phlebotomus kandelaki*) become infected with leishmaniae. In the digestive tract of the sandfly the leishmaniae multiply by division and assume a flagellated form. When they become numerous they move towards the anterior end of the digestive tract. If such a sandfly is crushed when it bites a healthy person, the leishmaniae may gain entrance into the human organism through the puncture left by the bite. Subsequently the parasites are carried by the blood flow and, after implanting themselves in the reticuloendothelial cells of the liver, spleen and bone marrow, lose their flagella and assume a round form. Leishmaniae multiply by simple division.

Pathogenesis and pathologic anatomy. As a result of long-continued parasitism of leishmaniae in the cells of the reticuloendothelial system (in the spleen, liver, lymph nodes and bone marrow) these cells undergo considerable degenerative changes and die. Although the reticuloendothelial cells proliferate at the same time, the newly formed elements are also affected by implanted leishmaniae. Simultaneously not only hyperplasia of the reticuloendothelial elements,

but also adipose degeneration of the parenchymatous organs takes place.

Dissection reveals considerable general emaciation of the people who have died of visceral leishmaniasis, oedema of subcutaneous tissue, haemorrhages in the intestinal wall, extreme enlargement of the spleen (of a saturated red colour) with splenic infarcts, enlargement of the liver and induration of lymph nodes in various regions.

Clinical picture. The incubation period lasts from 15 days to 5-6 months. The disease usually sets in gradually with indisposition, loss of appetite, irritability and a subfebrile rise in temperature.

On the 5th or 6th day of the disease the temperature rises considerably (to 39.5-40.5°C), although only for a short time. At each fall of temperature the patient perspires copiously.

Leishmaniasis is characterized by an irregular temperature curve with considerable variations not only over a period of several days, but also even in the course of one day. Between the various rises the temperature may be subfebrile.

As the disease progresses, the patient loses more and more weight and grows increasingly more anaemic, which becomes particularly noticeable from the 3rd or 4th month of the disease.

The progressing anaemia is accompanied by a sharp decrease in the number of erythrocytes and the amount of haemoglobin, which is soon followed by anisocytosis, toxic granularity of erythrocytes and erythroblastosis. Leucopenia and thrombopenia are also characteristic, the leucocyte formula shows relative lymphocytosis and monocytosis.

The spleen is usually enlarged from the very first days of the disease. Subsequently it continues to enlarge (Fig. 51) and may reach an enormous size (sometimes it descends into the minor pelvis). Palpation of the spleen in visceral leishmaniasis patients who have had the disease for over 3-4 months demonstrates that it is very compact and painless.

Visceral leishmaniasis usually runs a subchronic or chronic course. If the disease has entered the chronic stage (especially in neglected cases and in cases with no appropriate chemotherapy) extreme cachexia usually develops. During this period the patient has a characteristic appearance: he is extremely emaciated, the complexion is sallow, the subcutaneous adipose tissue is feebly marked, the lower extremities are oedematous, the abdomen is sharply inflated and the spleen is considerably enlarged. Exhausting diarrhoea is attended with a discharge of mucus and blood (streaks).

Owing to the sharp reduction in their general resistance visceral leishmaniasis patients, especially during the cachectic period, are uncommonly susceptible to various pyodermas; they often develop trophic ulcers.

There are also very mild forms of visceral leishmaniasis; in such cases the patients recover even when untreated.

The complications of this disease include haemorrhages into various organs, bedsores at points of the greatest pressure on the skin, trophic ulcers, otitides, mastoiditides and pneumoniae. These complications are due to the considerable emaciation of the organism, its lowered resistance, and disorders of the haematopoietic functions. Now and then a spontaneous rupture of the spleen is

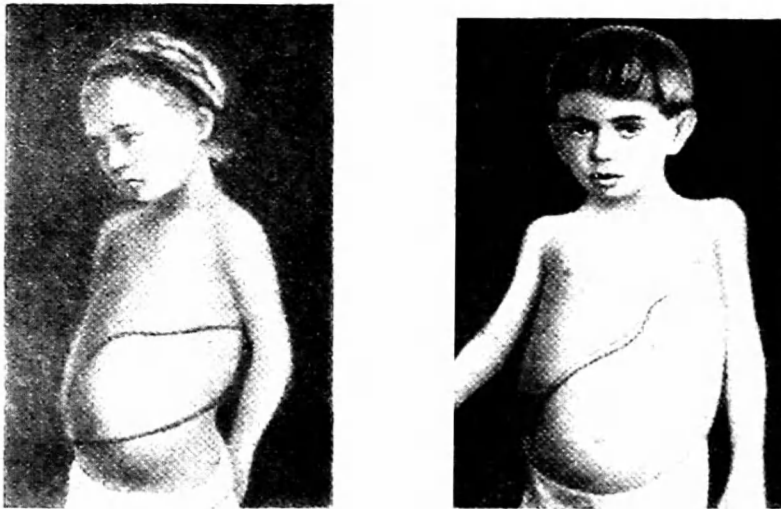


Fig. 14. Children affected with visceral leishmaniasis

observed; this severe complication is accompanied by acute loss of blood and development of collapse and requires an urgent operation.

An attack of visceral leishmaniasis confers lasting immunity.

Diagnosis. Epidemiological data and the clinical picture of the disease usually make it possible to establish a diagnosis. The diagnosis is based on temperature variations (two or three times a day with chills during the rise in temperature and sweating during its fall), considerable enlargement of the spleen, progressive loss of weight, characteristic changes in the blood picture and appropriate epidemiological factors (sojourn in areas where there are cases of visceral leishmaniasis).

Microscopic discovery of leishmaniae in a thick drop or smear of the patient's blood stained by the Romanovsky-Giemsa method serves as an authentic confirmation of the diagnosis. Many smears have to be examined because the peripheral blood contains but few leishmaniae and the latter are discovered only by examination of many fields of vision.

Leishmaniae can be seen the most frequently in Romanovsky-Giemsa-stained smears from a specimen obtained by puncture of the sternal bone marrow with a special needle.

A formol test may play an auxiliary part in diagnosing visceral leishmaniasis. An addition of 2 drops of a 40 per cent formalin solution to 1 ml of the patient's blood serum results, if the diagnosis is correct, in turbidity and gelatinization of the serum, i.e., a positive formol test.

In unclear cases it is necessary to differentiate the disease from chronic myeloid leukaemia and malaria.

Chronic myeloid leukaemia is accompanied by leucocytosis and a pathologic change in the leucocyte series beginning with myeloblasts, promyelocytes, myelocytes and juvenile cells.

Malaria is characterized by periodicity of the febrile attacks (mainly tertian and quartan malaria), slower and not so strongly pronounced development of such symptoms as enlargement of the spleen, hypochromic anaemia, leucopenia and lymphocytosis; repeated examinations of thick drops and smears of the patient's blood stained by the Romanovsky-Giemsa method make it possible to find plasmodia in malaria patients.

In neglected and in irrationally treated cases, as well as in cases where treatment was instituted late, the prognosis is usually serious, especially if the patients are emaciated or the disease is accompanied by purulent complications. In children the disease usually runs a more severe course than in adults.

In cases where vigorous treatment was instituted in due time the patients recover.

Treatment. Visceral leishmaniasis patients are treated with solusurmine (sodium salt of pentavalent antimony with gluconic acid). Twenty per cent solutions of solusurmine are prepared in twice distilled water and sterilized directly before administration.

Doses of 20 per cent Solusurmine Solutions for the Treatment of Visceral Leishmaniasis (in ml of Solution per 1 kg of the Patient's Weight)

Groups of patients	First administration	Second administration	Third and subsequent administrations
Children under 10 years (normal nutrition)	0.25	0.5	0.75
Children (dystrophic), affected with concurrent diseases	0.2	0.4	0.6
Children past 10 years and adults	0.2	0.2	0.5

Note: In cases where no appreciable improvement in the condition of the patients is observed after 8-10 injections the dose is increased to 1 ml of the 20 per cent solusurmine solution per 1 kg of the patient's weight and 2-3 additional injections (one injection per day) are made.



Fig. 52. Pavlovsky's protective (repellent) net

The injections are made daily for 12-15 days. Adults are administered the daily dose in two injections.

One 12-day course of solusurmine treatment usually suffices; in cases of an incomplete therapeutic effect a second similar course of treatment is administered 1.5-2 months after the end of the first course.

The chemotherapeutic effect produced by solusurmine and the completeness of recovery from visceral leishmaniasis are evaluated by the following indices: (1) considerable improvement in the patient's condition, appearance of good appetite and normal sleep; (2) complete normalization of the temperature and no temperature elevations for the following 1.5 months; (3) clear contraction of the theretofore enlarged liver and spleen; (4) normalization of the morphological blood picture and appreciable increase in haemoglobin; (5) absence of leishmaniae in microscopically re-examined specimen obtained by puncture of the sternum and stained by the Romanovsky-Giemsa method.

In cases accompanied by purulent complications the patients are given penicillin injections in addition to the main treatment of visceral leishmaniasis (for example, with solusurmine). General

roborant therapy must be widely utilized (transfusions of 150-200 ml of blood every 3 days, peroral administration of iron and phosphorus preparations, vitamin B₁₂, adequate diet enriched by animal proteins and vitamins).

Prevention. In the control of visceral leishmaniasis the main efforts in the foci of this disease must be aimed at exterminating the infected dogs and sandflies (vectors of this infection). Thorough cleaning of dwellings, production buildings and yards, ridding them of all refuse with subsequent disinfection with a 10 per cent calcium chloride solution ensures extermination of the larvae of sandflies.

In addition to the above it is necessary to provide the people with protection against sandfly bites, for which purpose flypaper is hung inside dwellings, the premises, especially the windows, are dusted with a 10 per cent DDT or hexachlorane powder, the windows are screened with a fine metal meshwork, the doors are kept closed by means of springs and are screened with gauze. The beds are protected with a gauze mosquito net. In some cases Pavlovsky's nets (Fig. 52) impregnated with sandfly-repelling solutions are worn. The exposed parts of the body may be painted with insect-repelling solutions (for example, dimethylphthalate).

PAPPATACI FEVER (*FEBRIS PAPPATASII*)

Pappataci or *sandfly fever* is an acute infectious disease caused by a filtrable virus and transmitted through bites of *Phlebotomus* sandflies (*Phlebotomus pappatasi*); the disease is accompanied by a temporary febrile reaction, sharp headache, conjunctivitis, characteristic injection of the sclerae and marked muscular pains.

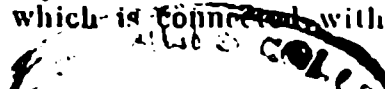
Brief historical information. Pappataci fever was known under various designations (for example, "three-day fever") as early as the beginning of the 19th century. In 1886 Pick (in Herzegovina) established the nosological entity of this disease and gave it a classical description. The role of *Phlebotomus* sandflies as the vectors of the infection was demonstrated in 1905.

In Russia this disease was for the first time described in greatest detail by Y. I. Martsinovskiy in the Caucasus in 1915. Academician E. N. Pavlovskiy, one of the most prominent Soviet scientists, found the disease to have its natural foci.

Aetiology. The disease is caused by a filtrable virus (*Febrigenes pappatasi*) which circulates in the blood of patients at the end of the incubation period and during the first two days of the disease.

The virus of pappataci fever is cultivated on the chorioallantois of the chick embryo. It has been possible to infect monkeys, which circumstance is utilized in elaborating a number of problems of pappataci fever pathology. The virus is very unstable in the external environment and is quickly destroyed by antiseptic substances.

Epidemiology. Pappataci fever has clearly defined natural foci and is noted for its seasonal occurrence, which is connected with



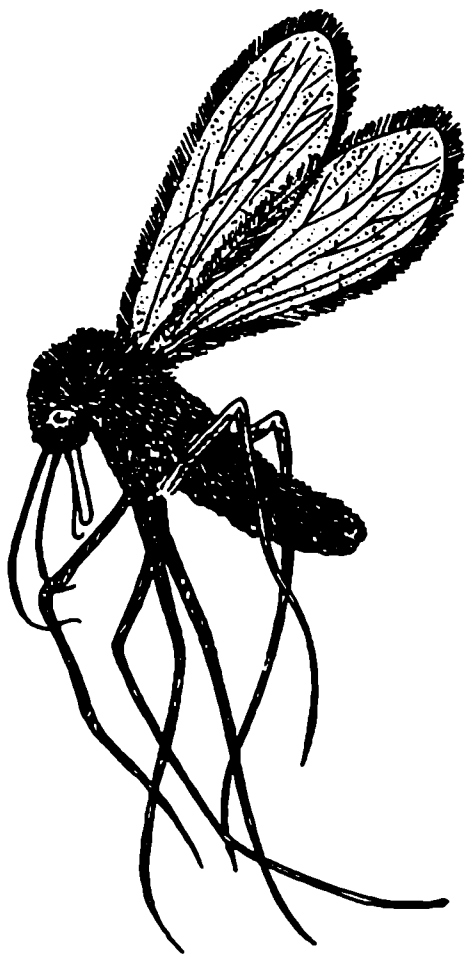


Fig. 53. Sandfly—*Phlebotomus pappatasi* (greatly magnified)

the definite conditions of habitat and biological activities of the *Phlebotomus pappatasi*, the vector of the disease (Fig. 53). Owing to this the disease may be observed only in certain areas. The sandflies settle near human dwellings and bite people at night.

The phlebotomus sandfly female is 2-2.5 mm long. From 7 to 10 days after sucking the blood of a person infected with pappataci fever sandflies become contagious; the above period is necessary for the virus to multiply.

The sandflies are contagious only at a temperature of above 18 C.

An attack of the disease confers unstable immunity, and reinfection during the same summer season is possible.

On the territory of the USSR pappataci fever occurs in Central Asia, the Caucasus and a number of areas along the Black Sea Coast.

Clinical picture. The incubation period is 3-8 days (it averages 4-5 days). A primary affect appears at the site of the sandfly bite and persists for a rather long time. The incubation is now and then followed by a short prodromal period which manifests itself in general indisposition, weakness, loss of appetite, and headache.

As a rule, pappataci fever sets in acutely. After a rather intense cold fit the temperature rapidly rises to 39.5-41 C. The patients complain of sharp headache, the ache being felt particularly in the region of the forehead and the top of the head, pain upon movement of the eyes and upon pressure on the eyeballs.

Taussig's sign is characteristic: raising the upper lid with the fingers produces sharp pain.

The patient's face is hyperaemic, the vessels of the conjunctiva

of the lids are filled with blood and the conjunctiva is therefore bright-red, the vessels of the sclerae are injected over a triangular area pointing towards the cornea in the outer corner of the eye (Pick's sign—Fig. 54).

The very frequently observed symptoms include sharp pains in the gastrocnemius muscles, in the back and the sacrum, hyperaemia of the fauces and oedema of the uvula and palatine arches.



Fig. 54. Pick's sign in pappataci fever patient

Sometimes patients have a liquid stool containing mucus. In many cases the pulse rate lags behind the temperature level. Examination of the cerebrospinal fluid obtained by puncture and exuding under elevated pressure reveals positive Nonne-Apelt's and Pandy's reactions.

The changes in the blood picture are characterized by leucopenia with a decrease in the number of lymphocytes, neutrophilic shift to the left and aneosinophilia; the ESR is 6-8 mm.hr.

The febrile period lasts three days, rarely longer (Fig. 55). As a rule, the temperature begins to fall on the second day of the disease and reaches the normal level by the beginning of the fourth day; after this the pain sensations disappear, and the appetite and sleep are restored. However, recovery is slow and sometimes takes several weeks, the working capacity is restored slowly. Some convalescents exhibit trophic disorders: loss of hair, fragility of nails or disturbance in their growth.

From 2 to 5 days after the end of the febrile period patients may suffer relapses.

Mild, effaced and atypical cases of the disease are possible; in these cases the febrile period lasts but 1-2 days.

Pappataci fever usually runs a favourable course; lethal results are extremely rare.

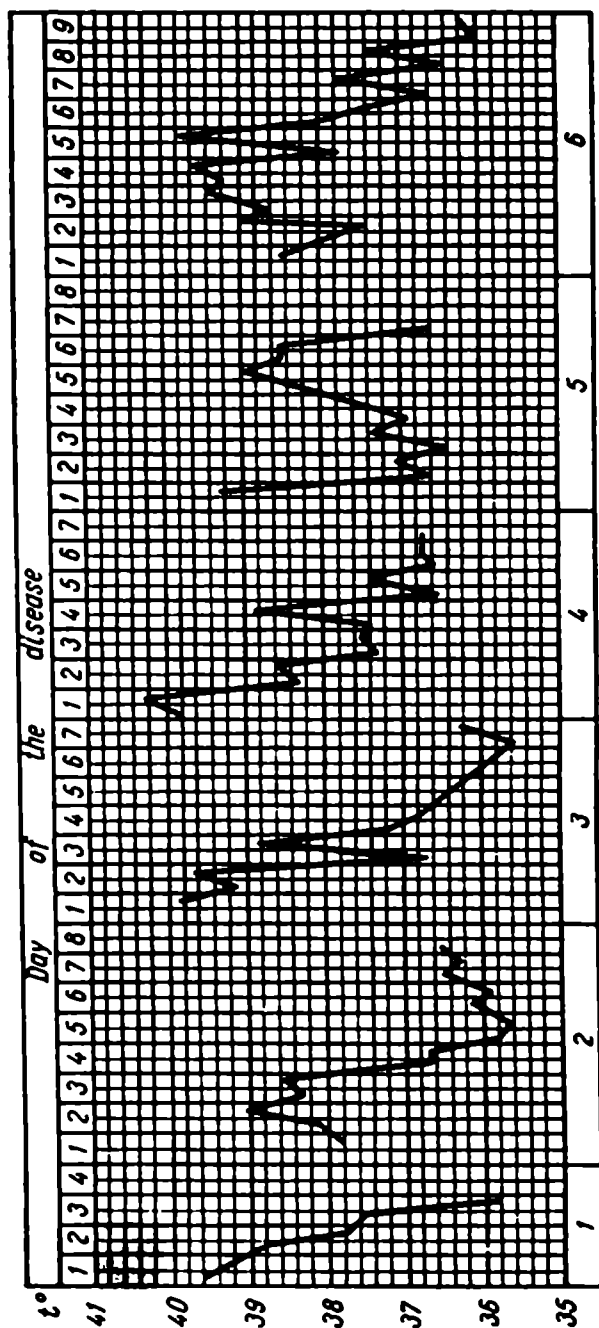


Fig. 55. Temperature curves in pappalaci fever

Diagnosis. Typical cases of pappataci fever with appropriate epidemiological data are quite easy to diagnose.

Differential diagnosis. The disease must be differentiated from influenza, typhus and tick-borne relapsing fever.

It should be remembered that in influenza there are no such characteristic signs as Pick's and Taussig's syndromes, and no sharp pains in the gastrocnemius muscles. In influenza there are pains in the supraorbital arches and the eyes (upon movement); some patients have catarrh of the nasopharynx, larynx and trachea.

Tick-borne relapsing fever which occurs only in certain foci is characterized by an acute onset following very intense chills and early enlargement of the spleen; examination of a fuchsin-stained thick drop of the patient's blood taken during an attack reveals spirochaetes.

During the first three days of typhus the face is not only hyperaemic, but also puffy, the pulse corresponds to the temperature level, petechial haemorrhages are possible in the retrotarsal fold of the conjunctiva (Chiari-Avtsyn sign), and the percussion borders of the spleen are extended.

Treatment. Only symptomatic agents are now used for the purpose of mitigating the pains. The patient must have bed rest and be given plenty to drink.

Prevention. To prevent pappataci fever, it is necessary to control the breeding of sandflies, which is a measure of social character, and to provide individual protection against their bites.

The breeding places of sandflies must be dusted with a 10 per cent DDT powder, the windows must be dusted with a 10 per cent DDT or hexachlorane powder, and strips of flypaper must be hung in dwellings and production buildings. The windows must also be screened with fine metal meshwork, special anterooms must be built at entrances to houses, mosquito nets must be hung over beds, and people must wear Pavlovsky's protective nets impregnated with sandfly-repelling substances.

Sandflies attack man before sunset and at night. For protection against their bites the exposed parts of the body should be painted with a 20 per cent alcohol solution of dimethylphthalate in the evening; a single painting of the face, neck and hands requires about 5 ml of the above solution; the protection lasts about 2-5 hours.

Methods of specific prevention by vaccination are now being elaborated.

HAEMORRHAGIC FEVERS

The concept of *haemorrhagic fevers* unites a group of acute infectious diseases with a febrile reaction and various haemorrhages. These fevers are divided into separate nosological forms in accordance with the clinical course, characteris-

tics of the causative agent and the geographic region of their occurrence conditioned by their natural foci.

The following haemorrhagic fevers are known: (a) haemorrhagic fever with a renal syndrome, also known as haemorrhagic nephrosonephritis or Eastern haemorrhagic fever; (b) Crimean haemorrhagic fever; (c) Omsk haemorrhagic fever.

The Soviet scientist M. P. Chumakov and a number of other investigators have made an important contribution to the study of haemorrhagic fevers.

Aetiology and epidemiology. Each of the aforementioned diseases is caused by a special strain of filtrable virus, has definite natural foci and definite reservoirs and vectors of the virus (various species of ticks). The mechanism of human infection with each of these fevers has its own peculiarities.

The virological characteristics of the causative agents of this group of infectious diseases are not very well known as yet. The natural foci of haemorrhagic fevers completely depend on definite climatic, geographical and other conditions which favour the existence of the vectors of the infections.

Pathogenesis and pathologic anatomy. The most important manifestations of these diseases are connected with severe affections of the capillaries of various organs, the skin and mucous membranes. Eastern haemorrhagic fever is characterized by severe affections of the glomeruli and renal tubules.

Clinical picture. Owing to the similarity of the clinical manifestations of the different diseases composing this group it is necessary to consider them by way of comparison.

(A). The clinical picture of so-called Eastern haemorrhagic nephrosonephritis (*haemorrhagic fever with a renal syndrome*) is characterized by symptoms of severe affection of the kidneys (the blood pressure may rise but slightly) with a marked pathologic character of the urine (protein, erythrocytes, casts). The incubation period averages 15 days with variations from 11 to 23 days.

The onset of the disease is marked by a prodromal period with the patients usually up and about (general weakness, indisposition, diminished appetite).

The febrile period begins with chills and a rapid rise in temperature to 39.5-40.5°C, which persists for 2-6 days.

The initial period of the disease, from the rise in temperature to the first haemorrhagic manifestations, is 2-4 days; general toxic phenomena, in a number of cases with meningeal symptoms, prevail.

The patients complain of headache, feeling of thirst, pains in the muscles and in the small of the back. The consciousness is often clouded, positive Kernig's and Brudzinski's signs are observed, the occipital muscles are rigid. The patient's face is hyperaemic, the vessels of the conjunctivae of the lids and of the sclerae are filled with blood. Signs of renal affection (pains in the small of the back, positive Pasternatsky's sign) appear early, although marked symptoms of renal pathology arise later.



Fig. 56. Eyes of haemorrhagic fever patient with renal syndrome. Haemorrhage into sclerae

The blood picture is characterized by leucopenia, aneosinophilia and band-cell shift of the neutrophils to the left.

The cerebrospinal fluid obtained by puncture exudes under elevated pressure and contains an increased amount of protein.

Clinical course of the disease. Between the 3rd and 5th days the disease enters the period of its highest development, the condition of the patients changes for the worst, the patients vomit, bleed from the nose and gums, and a petechial eruption appears on the lateral surfaces of the chest and in the region of the shoulder girdle. During this period the patients are sluggish and apathetic, complain of headache, sharp pains in the small of the back and the abdomen; the consciousness is often clouded.

The mucous membranes of the palate and lower lip exhibit enanthema (petechial haemorrhages), haemorrhages into the sclerae are also possible (Fig. 56); severe cases may be accompanied by apoplexy of the adrenals. Signs of haemorrhagic diathesis are strongly pronounced and the capillaries become more fragile. During this period of the disease, at least from the fourth day, the blood picture is characterized by moderate hypochromic anaemia, slight leucocytosis and neutrophilia with a shift to the left. Thrombocytopenia is characteristic of the febrile period. Pasternatsky's sign is clearly positive, and oliguria, which sometimes reaches the state of total anuria, is observed. The condition is marked by low specific gravity of the urine (1008-1002), haematuria and albuminuria. The amount of protein in the urine may reach 20-24^g _{mm}; the urine is the colour of meat slops (because of macrohaematuria).

In haemorrhagic fever with a renal syndrome the febrile period lasts about 8-9 days; at the end of it the temperature falls by an accelerated lysis in 2-3 days.

After normalization of the temperature the patient's condition continues to be grave; the patient vomits repeatedly and the renal disturbances are even intensified; anuria, considerable albuminuria and haematuria develop, and waxy, granular and fibrinous casts are found in the urine which has low specific gravity.

The nonprotein nitrogen in the blood is considerably increased, and uraemia is possible; the latter sometimes leads to a lethal result. The increase in nonprotein nitrogen is possible within 150-200 mg%.

Between the 4th and 6th days after normalization of the temperature the patient's condition improves and the patient begins to recover.

The blood picture is normalized 3-4 days after the fall of the temperature, albuminuria is eliminated between the 12th and 14th days from the beginning of the disease, but casts, including fibrinous casts, may be found in the urine over a longer period. The period of convalescence is marked by polyuria.

Most cases end in recovery, but the prognosis may be serious, and sometimes the disease may end lethally. The lethality varies within very wide limits and in severe cases of the disease may reach high figures.

(B). *Crimean haemorrhagic fever*, first studied by M. P. Chumakov and his associates in the summer of 1944 in the steppes of the Crimea, is an acute infectious disease which sets in suddenly with chills, vomiting, headache and a considerable rise in temperature. The face is hyperaemic, the vessels of the conjunctiva of the lids, sclerae, soft palate and uvula are injected. A number of haemorrhagic symptoms—petechial eruptions on the skin and mucous membranes, nasal haemorrhages, vomiting and stool containing blood, and haematuria—arise on the 4th or 5th day of the disease; in many cases the gums bleed, while women develop uterine haemorrhages. Examination of the patients reveals a labile pulse, dull heart sounds and arterial hypotension. The spleen enlarges only in some patients. Severe cases of the disease are accompanied by extreme dryness in the mouth, abdominal pains and recurrent liquid stool containing blood; the blood changes to melen, for the most part in the intestine.

The morphology of the blood is characterized mainly by a shift of the neutrophilic cells to the left, moderate lymphocytosis and normal ESR. The total number of leucocytes remain normal or may be slightly increased in individual patients.

(C). *Omsk haemorrhagic fever* is characterized by milder haemorrhagic phenomena than the first two forms (A and B) and runs a rather favourable course, although it may also produce lethal results. During the first days of the disease the temperature rises to 39-39.5°C. Half the number of patients exhibit febrile waves separated by afebrile periods which last 3-10 days.

The various forms of haemorrhagic fevers may be diagnosed on the basis of the clinical picture of the disease and epidemiological data (occurrence of the disease in the given area and its natural foci). Laboratory diagnosis is complicated and possible only in well-equipped laboratories.

Treatment. All patients must be hospitalized and given the best

possible care. They must be prescribed liquid, easily assimilable and highly caloric food with a maximum of vitamins, especially C and B (fresh vegetables and fruit, natural fruit and berry juices, sweetbrier infusion, and yeast). It is advisable to give patients per os 400-500 mg of ascorbic acid daily and, because of the haemorrhagic phenomena, vitamin K (vicasol—bisulphite derivative of 2-methyl-1,4-naphthoquinone [water-soluble analogue of vitamin K₂]) in a dose of 0.015 g 4 times per day for 4 days.

It should be remembered that the haemorrhagic manifestations may reach the acme not during the febrile period, but after its end.

Intravenous infusions of glucose (40-50 ml of a 40 per cent solution) must be also administered. Transfusions of 125-150 ml of blood every other day and intramuscular injections of campolon (aqueous liver extract) or antianæmin (cobalt-containing liver extract) in a daily dose of 2 ml for 5-7 days and iron preparations per os are recommended during the febrile period. Dimedrol (diphenhydramine), an antihistaminic preparation, must be given in a dose of 0.08 g 4 times per day for 4-6 days as an auxiliary therapeutic agent. Convalescents must have bed rest until the symptoms have completely disappeared; after discharge from the hospital the patients need medical observation.

Prognosis. The severity of the clinical course of haemorrhagic fevers varies very widely. Eastern nephrosonephritis runs a much severer course than the other afore-described haemorrhagic fevers and in some cases ends lethally.

Prevention. The success in the control of haemorrhagic fevers is determined by the results of the measures aimed at exterminating the vectors of the infection and at protecting healthy people against their bites. In areas where these diseases occur it is necessary thoroughly to clear the plots allotted to dwellings and production buildings by mowing the grass, destroying the shrubs and burning the fallen leaves.

People living or working in areas where haemorrhagic fevers occur must wear boots, gloves and special coveralls; the working clothes must be impregnated with tick-repelling substances. The necessity for carrying out these measures depends on the concrete epidemiological situation. The afore-mentioned agents ensure protection against the bites of infected ticks which are vectors of haemorrhagic fevers.

For specific prevention of Omsk haemorrhagic fever in the natural foci of this disease a prophylactic vaccination with an emulsion of the virus killed by formalin is administered.

The main role in the prevention of haemorrhagic fevers is still played not by vaccination, but by the above-described measures systematically carried out.

EPIDEMIC ENCEPHALITIDES

The group of epidemic encephalitides includes infectious diseases caused by various strains of filtrable viruses and characterized mainly by affection of the brain. The various diseases of this group differ in their clinical pictures, pathogenesis and routes of transmission.

Although encephalitides have long been known to medical practice and have even been described under various designations, the scientific study of these diseases produced positive results only in 1917-1922 when an epidemic of lethargic encephalitis broke out in Europe. It was then that Economo first described the clinical aspects of this disease.

Seasonal encephalitides whose spread is closely connected with the biological characteristics of the vectors of the infections and the natural foci of these diseases were studied later, in the 1930's.

The following forms of encephalitis are usually distinguished today: *epidemic type A encephalitis* (Economo's lethargic encephalitis described in courses of nervous diseases) and *a group of seasonal encephalitides* which include, among others, the spring-summer (taiga) tick-borne encephalitis and the summer-autumn (Japanese) mosquito-borne encephalitis.

Seasonal Encephalitides

1. Tick-Borne Spring-Summer (or Taiga) Encephalitis (Encephalitis Acarina Orientalis)

Brief historical information. Spring-summer encephalitis undoubtedly occurred in certain areas, in accordance with natural foci, even in hoary antiquity.

In 1935 the Soviet investigator A. G. Panov gave the first clinical description of this disease, while in 1937 combined expeditions working in taiga areas of Eastern Siberia under the supervision and with the participation of E. N. Pavlovsky, A. A. Smorodintsev, L. A. Zilber, V. D. Solovyov and others made a detailed study of the epidemiology, clinical picture and prevention of this disease. The isolated strains of the causative agent—filtrable virus—were then thoroughly studied. Specific methods to prevent the disease by viral vaccination are now being elaborated.

Aetiology. The disease is caused by a special strain of filtrable virus (*Encephalophilus silvestris*) pathogenic to man and certain species of monkeys. Heating to 100°C and the action of various disinfectants terminate the vital activities of the virus; the virus is unstable in the external environment.

Epidemiology. The disease has *natural foci*, i. e., it needs for its spread a certain aggregate of climatic and soil conditions, an appropriate vegetation and landscape which make possible the existence of pasture ticks—the vectors of the infection.

Tick-borne encephalitis occurs not only in taiga areas, but also in other regions which are natural foci of the infection; economic exploitation of forests in these foci may be accompanied by occurrence of this disease.

Chipmunks, grey rats, field mice and other rodents are the main reservoir of the virus in nature, while *Ixodes persulcatus*, and less frequently *Dermacentor silvarum* and *Ixodes ricinus* ticks inhabiting the coniferous taiga, broad-leaved and mixed forests serve as an auxiliary reservoir and as carriers of the infection from the infected rodents to man. The ticks can also exist in forest-steppe areas and are able to retain the virus for a long time. The virus is retained in nature by transmission of the microorganisms from the rodents to the ticks, who feed on them, and back. Various forest birds on which the ticks parasitize may also serve as a reservoir of the infection.

The seasonal incidence of the disease is closely connected with the periods of the greatest biological activity of the vectors of the infection. During the spring-summer period (May-June) the ticks attain complete maturity and, being infected, may transmit the infection to man by biting him and sucking his blood.

Pathogenesis and pathologic anatomy. By moving with the blood flow from the site where man was bitten by an infected tick the filtrable virus which causes the disease quickly reaches the cells of the central nervous system, lodges in them and produces degenerative changes.

The virus particularly affects the nerve cells of the ventral horns of the cervical division of the spinal cord and the nuclei of the medulla oblongata where it produces necrotic and dystrophic changes in the nerve cells and is responsible for neuronophagia.

Clinical picture. The incubation period lasts an average of about two weeks, varying from 8 to 20 days. The disease sets in acutely. After slight chills the temperature rises in the course of one day to 39.5-40 C and persists at that level for 5-7 days. At the end of the febrile period the temperature falls critically or by accelerated lysis. About one-third of all cases are accompanied by a two-wave temperature curve.

During the first 2-3 days the patient has sharp headaches, is generally jaded, and vomits repeatedly. Examination of the patient reveals hyperaemia of the face and the conjunctivae. In severe cases the consciousness is clouded and meningeal symptoms (rigidity of the occipital muscles, Kernig's and Brudzinski's signs) are observed. The patient's blood exhibits aneosinophilia and lymphopenia. Inhibition, sleepiness and relative bradycardia are often noted.

The cerebrospinal fluid is transparent; it flows out under elevated pressure and contains more protein and formed elements than normally; Pandy's test is positive. Meningeal forms of the disease are not infrequent.

Some patients develop flaccid paralyses of the upper extremities and the muscles of the neck on the 2nd or 3rd day of the disease.

Severe cases are marked by such pathologic phenomena as inarticulate speech, choking and deglutition difficulties due to affection of the nuclei of the 9th, 10th and 12th pairs of cranial nerves in the brain stem.

The fall of the temperature is followed by a period of convalescence, but far from all patients completely recover their motor functions; some people who have survived an attack of spring-summer encephalitis retain permanent paralyses.

Sometimes tick-borne encephalitis occurs in atypical or very mild forms, but permanent flaccid paralyses may develop even in these cases.

An attack of the disease confers lasting immunity.

Prognosis. In most cases the prognosis as regards the patient's life is favourable, lethal results being observed in 1-1.5 per cent of all cases; the patient may die on the 4th or 5th day of the disease or after the fall of the temperature. Some cases result in paralyses of the muscles of the neck and the entire shoulder girdle (Fig. 57).

Diagnosis. Tick-borne encephalitis may be diagnosed on the basis of epidemiological data (the patient's sojourn in an encephalitis focus, tick bites) and the clinical picture (acute onset of the disease

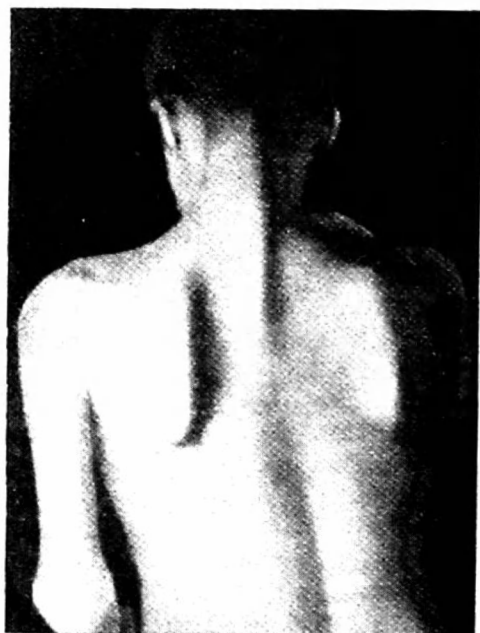


Fig. 57. Paralysis of muscles of the shoulder girdle in tick-borne encephalitis with phenomena of muscular atrophy; "angel's wings"

with a rise in temperature, meningeal phenomena, character of the cerebrospinal fluid, development of flaccid paralyzes of the upper extremities and neck between the 2nd and 4th days, and bulbar disorders in severe cases).

Differential diagnosis. The disease must be differentiated from epidemic meningitis, poliomyelitis, typhus and North-Asian rickettsiosis (tick-borne typhus).

The laboratory methods of confirming the diagnosis consist in virological tests: complement fixation test and discovery of virus-neutralizing antibodies in the serum of the patient's blood.

Treatment. A specific antiserum is now used in the treatment of tick-borne encephalitis (40-50 ml a day is administered intramuscularly for 2-3 days during early periods of the disease, the first injection being made by Besredka's method or by the method described above. See "Principal Methods of Treating Infectious Patients").

The above serum is obtained by immunization of horses with a culture of the virus which causes this disease.

The following auxiliary agents are recommended: daily intravenous infusions of 40 ml of a 40 per cent glucose solution, peroral administration of 0.05 g of dimedrol 3 times per day for 5-6 days and intramuscular injections of vitamin B₁—thiamine bromide—0.01-0.015 g once a day for 10-12 days.

Every patient needs thorough individual care. The patients are prescribed easily-assimilable high-calory semiliquid food containing a lot of vitamins, especially vitamin C and the B complex. Convalescents may not be allowed out of bed before 2 weeks have elapsed since the normalization of the temperature.

If flaccid paralyzes develop, it is necessary to administer physiotherapy and strictly supervised kinesitherapy.

Prevention. All persons working in natural foci of tick-borne (spring-summer) encephalitis must examine their clothing, underwear and body twice a day and destroy the sucked-up ticks. The tick can be easily removed by application of vegetable or vaseline oil to the site where it has sucked up.

For protection against tick bites it is necessary to wear special coveralls which completely cover the neck and hands; such coveralls are tightly closed in the back and have two rows of buttons in front. The collar and cuffs of the coveralls are painted with tick-repelling substances (dimethylphthalate or other repellents). It is necessary to wear rubber boots; if no rubber boots are available the trousers must be tucked into leather boots. In all human stopping places the grass and fallen leaves must be burned and all measures must be taken to exterminate the rodents. The areas infested with ticks must be sprayed with DDT or hexachlorane powders from aircraft.

Inoculations play an auxiliary role in preventing spring-summer encephalitis; they consist in subcutaneous administration of a

specific vaccine containing the causative agent—the filtrable virus of tick-borne encephalitis killed with formalin. The vaccine is administered in a dose of 2-3 ml at 7-day intervals; the immunity lasts up to 1 year. People living in areas with natural foci of this infection must be taught the necessary rules of hygiene.

2. Mosquito-Borne Summer-Autumn (Japanese) Encephalitis (Encephalitis Japonica)

The disease is caused by a special strain of filtrable virus (*Encephalophilus japonicus*) transmitted to a healthy person through mosquito bites. Six different species of mosquitos, including the *Aedes togoi* and *Culex pipiens*, serve as the reservoir and vectors of the infection. The disease occurs mainly in Japan, but cases of it have also been observed in the Far-Eastern regions of the USSR. The period of the end of summer and beginning of autumn, the time of the most intensive breeding of mosquitos, is the season of mosquito-borne encephalitis incidence. Domestic animals are observed to have this disease also caused by bites of infected mosquitos.

When an infected mosquito bites man, the filtrable virus penetrates into the blood circulation. The incubation period is 10-15 days. During the first five days of the disease the causative agent may circulate in the patient's blood and be contained in the cerebrospinal fluid.

The central nervous system is selectively affected by the virus with resultant oedema and acute inflammatory changes in both the white and grey matter of the brain. Usually the pathologic process also affects the meninges.

The disease begins with chills after which the temperature rapidly rises to 40-40.5°C. This is followed by sharp headaches, general jadedness, meningeal and encephalitic symptoms; the consciousness is often clouded.

In some cases the strongly pronounced general intoxication and general cerebral phenomena may be accompanied by comatose states or motor unrest. The disease runs a short clinical course and its symptoms develop very acutely. Blood tests show relative lymphopenia and aneosinophilia. The cerebrospinal fluid is found to have elevated pressure, increased cytosis and a growing amount of protein.

In favourable cases the temperature falls towards the 5th or 6th day of the disease, and the patient begins to recover. Severe cases may result lethally. Due to the absence of specific treatment mortality is still high.

Mild, atypical and effaced forms of encephalitis are sometimes observed; these forms are of no small importance to epidemiology. In establishing the diagnosis it is necessary to consider the patient's sojourn in an endemic area, the season, the presence of mosquito

bites and symptoms of the clinical picture with due regard for the cerebrospinal fluid.

Of the laboratory methods of diagnosis the complement fixation test and determination of the virus-neutralizing antibodies in the blood serum and the cerebrospinal fluid are used.

All patients must be hospitalized.

Treatment. Attempts have been made to use the antiserum (40-50 ml per day subcutaneously) obtained by immunizing horses with a culture of the causative agent, but owing to the insufficient effectiveness of the antiserum symptomatic therapy (intravenous glucose infusions, subcutaneous physiologic solution infusions, vitamins per os) has retained its importance. Peroral administration of 0.015 g of proserine (neostigmine) twice a day is advisable. Nutrient enemas are administered in cases of deglutition disorders.

Prevention consists in carrying out measures of individual protection against mosquitos (see "Malaria" and "Pappataci Fever"), petrolization of water reservoirs at mosquito breeding grounds, extermination of mosquitos by spraying DDT and hexachlorane emulsions and powders. The terrain around populated areas and stopping places must be thoroughly cleared.

In the foci of infection all persons who are in danger of infection must be inoculated with a vaccine prepared from the brain of mice infected with a standard strain of the virus of summer-autumn encephalitis; in this vaccine the virus is killed by formalin.

III.

ZOONOTIC INFECTIONS

The infectious diseases which attack not only man, but also some species of animals which transmit the disease to man are called *zoonotic infections*.

Of the various zoonotic diseases the most important role in human epidemiology is played by those which attack *livestock*, especially cattle.

Man contracts the disease from diseased animals either through close contact with them or consumption of their meat, milk and products made of this milk. In some cases the infection, for example, anthrax may be transmitted to a healthy person through things made of the skin, bristle and fur of infected animals.

Zoonotic infections affect mainly inhabitants of agricultural areas in some way or other connected with diseased animals. However, cases of zoonotic infections may be observed among people working in tanneries, furrieries, slaughterhouses and meat packing plants (anthrax). Townspeople who have nothing to do with agriculture may contract brucellosis by drinking the milk of a goat or cow infected with this disease.

The zoonotic infections also include rabies which is transmitted to man by animals through bites and salivation on even slightly damaged skin.

RABIES (HYDROPHOBIA, LYSSA)

Rabies is an acute infectious disease of zoonotic origin caused by a filtrable virus transmitted through bites of infected animals or their salivation on damaged skin; it is accompanied by affection of the central nervous system, convulsions, spasms of the pharyngeal and respiratory muscles, and terminates lethally in the stage of paralyses.

Brief historical information. The Russian scientist N. P. Vasilyev (1852-1891) demonstrated as early as 1876 that in rabies the pathoanatomic changes develop in the central nervous system. In 1881-1888 the great French scientist Louis Pasteur showed, by a series of brilliant experimental studies, that the rabies virus concentrates in the central nervous system, and developed a vaccine against this disease. Since then inoculations against rabies have been widely used in medical practice; made in due time after a bite or salivation by an infected animal these inoculations prove very effective.

Aetiology. The disease is caused by a special strain of filtrable virus (*Neuroryctes rabiei*) excreted in the saliva of rabid animals (mainly dogs, wolves and cats) and present in the cells of their central nervous system throughout the period of active manifestations of the disease. The presence of the virus in the central nervous system is confirmed by discovery of special inclusion bodies—Negri bodies—in ganglion cells; these bodies are reactive changes of the protoplasm of the nerve cells in which the virus parasitizes.

It had long been noted that the virulence of the causative agent of rabies present in the brains of infected animals and in their saliva varies very widely. By infecting a rabbit with an emulsion of the brain of a rabid dog and then repeatedly passing the virus through other rabbits it is possible, as was shown by Pasteur, to increase the virulence of the causative agent to a certain value, i.e. to produce so-called fixed rabies virus. If the substance of the spinal cord containing the fixed virus is taken from a rabbit infected by this method and is dried and treated with formalin or glycerin, the emulsion of this substance containing attenuated virus may be used for inoculations to people infected with rabies. This principle underlies the production of the rabies vaccine.

Epidemiology. Under natural conditions man becomes infected with rabies through bites by rabid animals or their salivation on damaged skin or mucous membranes (scratches, abrasions, cracks).

Rabid dogs, cats and wolves are the main reservoir of the virus and source of human infection; the epidemiological role of rabbit dogs is particularly important. The saliva of diseased animals contains the virus in various amounts and of various virulence.

Bites in the head, face and neck are particularly dangerous because in these cases the incubation period is much shorter and the disease runs an especially severe course. Bites of the covered parts of the body are less dangerous because the clothing may at least partly absorb the rabid animal's saliva containing the virus.

Rabies is a typical zoonotic disease and its epidemiology is therefore most closely connected with epizootology (prevalence of this disease among animals).

The most important part in the epidemiology of rabies is played by rabid dogs. Dogs may contract the disease by being bitten by each other and by rabid wolves. Cats may also be a source of infection.

In dogs the incubation period is 2-8 weeks. The first signs of the disease are restless and unusual behaviour, refusal of food and devouring of inedible things.

Soon the diseased dog develops a husky, howling bark, refuses to drink water, salivates copiously and has difficulties in swallowing. The period of extreme excitement, when the dog rushes about confusedly and tries to bite other animals or people, is followed by paralysis and death.

Sometimes dogs exhibit sullen rabies in which the period of excitement is short, the excitement is mild, but the paralyzes and the animal's death occur much sooner.

The animal suspected of rabies needs watching by veterinarians in order that they may reveal the earliest signs of the disease. As soon as symptoms of rabies appear the animal must be killed and its brain must be sent for examination to a histological laboratory of an antirabic division of a polyclinic or to a Pasteur station. Histological examination of the ganglion cells of the brain, especially in the area of the hippocampus, reveals numerous inclusion bodies—Negri bodies—specific of rabies.

Pathogenesis and pathologic anatomy. After gaining entrance through the atrium of infection (wound inflicted by the animal's bite, or scratch on the skin where the animal has deposited its saliva) the causative agent of the disease is carried by the fluid in the perineural spaces along the nerve trunks in the direction of the central nervous system. From the atrium the virus may also be carried by the lymph or blood.

The virus becomes fixed in nerve cells where it parasitizes and produces reactive changes of the cell protoplasm, resulting in formation of Negri bodies.

The virus accumulates mainly in the nerve cells of the hippocampus, medulla oblongata, cerebellum, nuclei of the cranial nerves, sympathetic ganglia and the lumbar part of the spinal cord. The affection of these parts of the nervous system gives rise to increased reflex excitability and convulsions, particularly strongly pronounced in the muscles of deglutition and respiration, increased salivation and perspiration. As a result of affection of nerve centres, paralyzes of the muscles of the extremities and of the heart develop during the late period of the disease; the paralysis of the heart leads to death.

Histological examination of the brains of people who have died of rabies reveals numerous haemorrhages, swelling and disintegration of the nuclei of nerve cells, vacuolization with fatty degeneration of their protoplasm, and Negri bodies (Fig. 58) in the cells of the hippocampus; the latter serve as an absolute confirmation of the diagnosis of rabies.

Clinical picture. The incubation period lasts from 15 to 55 days, and in some cases up to one year. It is followed by a prodromal period of 1-3 days. A dull, gnawing pain arises at the site of the rabid animal's bite even if the wound has already healed; in a number of cases this is followed by burning and hyperaesthesia around the wound. The patient is in a dejected mood, his sleep is disturbed and hallucinations of a threatening character sometimes appear. The disease lasts a total of 5-7 days, sometimes 10-12 days.

The course of the disease is usually divided into three stages: (1) the aforementioned prodromal stage, (2) furious stage lasting

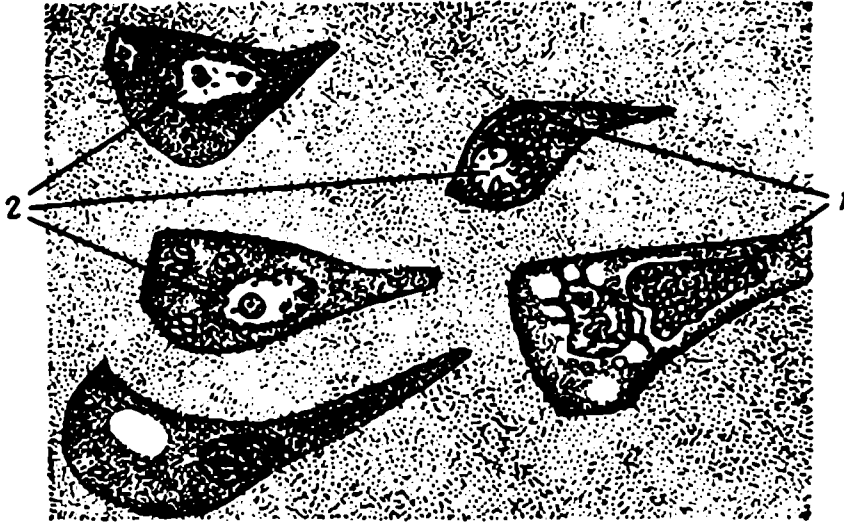


Fig. 58. Rabies. 1—Negri bodies in ganglionic cells of the brain; 2—cell nuclei

from 4-5 to 6-7 days, and (3) paralytic stage which soon ends in death.

The temperature rises to $37.2-37.3^{\circ}\text{C}$ and is followed by a disturbance in respiration. Inhalations become deep and noisy and involve all of the respiratory muscles; the exhalations assume a form of 2-3 spasmodic contractions of the diaphragm followed by a pause. The patient is excited, upset, and complains that he hasn't enough air.

Owing to the considerable tactile, auditory and visual hypersensitivity of the patient the slightest contact or noise, and bright light give rise to reflex clonic and tonic spasms.

Subsequently spasms appear spontaneously. If a cup of water is brought to the patient's lips, the mere sight of water evokes reflex spasms of the muscles of deglutition and, despite the tormenting thirst, the patient pushes the cup away. The difficulty in swallowing or even the inability to swallow liquid is characteristic of rabies patients; this symptom is absent only in very rare cases, for which reason the disease is also called *hydrophobia* (fear of water).

The continuously increasing reflex excitability leads to development of aerophobia (morbid fear of drafts or of fresh air).

From the second or third day of the disease the patient becomes loquacious with abrupt and incoherent speech, develops visual and auditory hallucinations which are often of a threatening character; the patient is excited and hyperactive, and salivates copiously.

Rabies is characterized by mental disturbances, namely, delusions of persecution and aggressive actions. Some patients crawl

on the floor, rend their clothes, scratch and bite themselves, and try to attack the people in their surroundings. In cases of extreme excitement the patients must be put to bed under a rope net; such patients need individual watching by the attending personnel.

The patient's consciousness clears up for a short period, but subsequently the spasms occur increasingly more frequently and the salivation becomes more copious.

The excitement stage is followed by the *paralytic stage* which lasts 10-24 hours. During this stage the patient develops paresis or paralysis of the lower extremities; paraplegia is observed more often than hemiplegia; the patient lies motionlessly in bed, mumbles incoherent words and from time to time jumps up.

The disease ends in agony and death.

The foregoing is a clinical picture typical of rabies, but there are also other variants of this disease, the most important of which are the following.

1. *Bulbar form*: the patient retains his consciousness, exhibits marked symptoms of affection of the medulla oblongata, dysphagia and respiratory disorders.

2. *Cerebromaniacal form*: this form is characterized by various delusions, maniac-depressive psychosis and comparatively rare spasms.

3. *Cerebellar form*: dizziness and unstable atactic gait.

4. *Paralytic form*: the patient very early develops paralyzes which run a course resembling that of mono-, hemi- and paraplegias, sometimes with a picture of ascending Landry's paralysis when increasing multiple paralyzes lead to severe disorders of external respiration and death.

It should be remembered that all of the foregoing clinical forms of rabies are characterized by spasms of the muscles of deglutition and symptoms of hydrophobia.

Prognosis. If the clinical picture is clearly that of rabies and the diagnosis is correct, the prognosis is always hopeless because no effective methods of treatment have as yet been found.

Diagnosis. A tentative diagnosis of rabies may be established already during the prodromal period on the basis of anamnestic data (bite or salivation by a rabid animal) and appearance of hallucinations. After the appearance of the main clinical symptoms (excitement, frequent hallucinations, aggressiveness and delusions, spasms of the muscles of deglutition, hydrophobia, general hyperaesthesia with increased reflex excitability, perspiration and copious salivation) the diagnosis becomes perfectly clear.

If the patient was taken under medical observation during the paralytic stage, i.e., the latest period of the disease, the diagnosis is based on the anamnesis, general succession in the development of the symptoms and presence of muscular paralyzes. It should be noted that in some cases there may not be any spasms of the mus-

cles of deglutition. It is necessary to bear in mind the afore-described variants of the clinical course of the disease.

Treatment and care of patients. Every rabies patient must be hospitalized and placed in a separate room; each patient needs individual care and observation. In cases of extreme excitement patients are put to bed under a net fastened to the bed. The attending personnel must beware of the patient's bites or his salivation on their skin and mucous membranes; there is very little danger of contracting the disease directly from the patient in any other manner.

In the patient's room there must be no drafts, bright daylight or artificial light, or shining objects which may evoke reflex spasms in the patient; there must be complete silence.

Since the patient cannot swallow, he is administered nutrient enemas; he may similarly be given a 5 per cent glucose solution. The tormenting convulsions and the patient's general excitement are eliminated by enemas containing chloral hydrate (2 g in 100 ml of starch decoction) and subcutaneous injections of morphine. There are no effective methods of treating rabies, but this must not diminish the concern and consideration of the medical personnel for the patient.

Prevention. The following measures are required for effective prevention of rabies: (1) prevention of infection of people by rabid animals, and (2) if infection has taken place, the patients must be given antirabic inoculations as early as possible (in the very beginning of the incubation period).

The first of these objectives is achieved by general extermination of wolves as the main reservoir of the rabies virus in nature and by preventing epizootics among dogs and cats. The spread of rabies among dogs is suppressed by permanent veterinary control and strict administrative and public measures consisting in the following: (a) compulsory administrative registration of all dogs; (b) extermination of all stray dogs; (c) muzzling of all dogs in populated areas; and (d) immediate extermination of all dogs showing even the earliest symptoms of rabies.

In the USSR there is a number of Pasteur (antirabic) stations and a wide network of Pasteur inoculation centres which are departments of hospitals and polyclinics. At Pasteur stations and centres all people bitten by rabid animals are vaccinated against rabies. The vaccine is prepared from an emulsion of the spinal cord of rabbits treated with a 1 per cent phenol solution (Fermi vaccine) or ground with anhydrous sterile glycerin (Phillips vaccine). The Fermi vaccine is usable for 5 months after its preparation, the Phillips vaccine—for 1.5 months.

The vaccine contains immunizing doses which vary with the degree of attenuation of its virulence.

During the many years of its use in different countries the vaccine has proved to be a reliable agent of rabies prevention.

It should be remembered that the inoculations confer immunity only 14-16 days after their completion, for which reason it is necessary to begin the course of inoculations as soon as possible after a person's infection. If the inoculations are administered in due time—within 14 days of the moment of infection—they prove to be effective. There are no contraindications for antirabic inoculations.

Persons with severe bites in the neck, face and head should be administered, in addition to the course of antirabic vaccinations, immune gamma-globulin (intramuscularly in a daily dose of 15 ml for adults).

If at the time of the bite or salivation on damaged mucous membranes the animal showed signs of rabies, the inoculations must be started immediately. Animals which showed no signs of rabies at the time of the bite are kept under observation for 14 days; at the first signs of disease in the animal it is necessary to start inoculations of the bitten person.

In cases of moderately severe bites the Fermi vaccine is administered subcutaneously in a dose of 6 ml per day for 15 days and then 3 ml for 10 days. The dose of 6 ml is administered in two injections of 3 ml one hour apart.

The Phillips vaccine is administered in increasing doses—from 0.5 to 2.5 ml (15 injections). The inoculations are administered according to certain instructions with due regard for the circumstances and atriom of infection; in cases of bites in the face, head and neck, and late inoculations (later than the fourth day after the bite) the dose and duration of the course of inoculations are increased and immune gamma-globulin is administered.

All persons bitten by animals (known to be rabid, fallen, killed or disappeared within 14 days after the bite) must be given a complete course of inoculations.

It is also necessary to inoculate all persons bitten by animals of healthy appearance but suspected of disease and kept under veterinary observation. In cases of scratches on the skin or mucous membranes made by claws of a rabid animal and in all cases of salivation on the skin or mucous membranes by an animal suspected of rabies it is necessary to administer a full course of antirabic inoculations.

Inoculations are also made if it was impossible, for some reason or other, to examine for Negri bodies the brain of the dog which bit the person and showed signs of the disease.

Usually the inoculations begin with more massive doses of the vaccine, which are then reduced in accordance with established schemes. The rabies vaccine is administered into the subcutaneous tissue of the abdomen daily for 25-40 days. In cases of most dangerous bites in the head or face it is necessary to administer one more (short) course of inoculations 10-15 days after the end of the first course.

During the period of inoculations and for 6 months afterwards consumption of alcohol is categorically prohibited because it reduces the effects of the vaccination and prevents the development of immunity.

BRUCELLOSIS

Brucellosis is a general infectious disease of zoonotic origin: it is caused by one of the three species of causative agent (brucellae) mentioned below; the disease develops when the causative agent enters through the gastrointestinal tract, damaged skin or mucous membranes.

The disease is characterized by a protracted febrile reaction, affection of the supportive and motor apparatus, enlargement of the liver and spleen, a number of typical complications and relapses with a possible generalization of the infection (bacteraemia) during its aggravations.

Brief historical information. Although the disease undoubtedly occurred even in antiquity, the first scientific description of it was made by Murstone, English army physician, only in 1861.

In 1886 David Bruce, an English army physician in Malta, discovered the causative agent of the disease in the spleen of a person who had died of brucellosis (Malta fever) and one year later obtained a pure culture of brucellae.

The causative agent of infectious abortion of cows, which also belongs to the group of brucellae, was discovered by Bang in 1897, while the causative agent of infectious abortion of hogs was discovered by Traum in 1914. Later all three strains were given the common designation of brucellae in honour of Bruce.

In 1897 Wright suggested a serological agglutination test for the diagnosis of brucellosis and in 1922 Burnet developed an allergic intradermal test which facilitates the diagnosis of the disease.

In Russia the studies of brucellosis were initiated by Y. I. Martsinovsky (1911), but the disease began to be investigated in detail in various parts of the USSR only in 1935. Soviet scientists (P. F. Zdrodovsky, P. A. Vershilova, G. A. Pandikov, V. N. Beklemishev, G. P. Rudnev and others) have now elaborated a number of important problems concerning the pathogenesis, clinical aspects, therapy and prevention of brucellosis. The Soviet Union uses an extensive system of measures in the control of this infection.

Aetiology. Three different strains of brucellae (causative agent of brucellosis) cause the disease in man and livestock: *Brucella melitensis* (sheep and goats), *Brucella abortus bovis* Bang (cattle, mainly cows) and *Brucella abortus suis* (hogs).

Morphologically all these microbes are identical and may be differentiated on the basis of the following characteristics: (1) different reaction to the bacteriostatic action of dyes (methyl violet, fuchsin, thionine and pyronin); (2) different ability to form hydrogen sulphide while growing on liver agar; (3) different carbon dioxide requirements when cultivated in artificial nutrient media.

Brucellae have the form of short rods, sometimes spheres (coccoid); they are 0.5-2 μ long and 0.3-0.5 μ wide and are easily stained with various aniline dyes.

In the first generation (primary inoculation in liver broth) the brucellae grow very slowly (18-25 days). In the external environ-

ment the brucellae exhibit considerable resistance and very well tolerate cold and even freezing.

Boiling kills brucellae in 1-2 minutes. The most destructive disinfectants are chloramine and hydrochloric acid; a 5 per cent calcium chloride solution kills brucellae slowly (within 12 hours).

Humans are most commonly infected with goat-type brucellosis (*Brucella melitensis*).

Epidemiology. Under natural conditions brucellosis attacks livestock, mainly sheep, goats, hogs and cows.

In these animals brucellosis runs a symptomless course or is accompanied by a febrile reaction, development of mastitides (especially in goats), arthritides and abortions. In the afore-said animals the disease is revealed by allergic skin tests and serologic tests.

The spread of brucellosis among humans is closely connected with its spread among animals, i.e., is determined by the epizootological peculiarities of local conditions.

Man may contract the disease primarily by consuming raw milk, inadequately cooked or fried meat of brucellose animals, and products made from the milk of infected animals.

With such most commonly observed *enteral* route of infection brucellosis may be contracted not only by inhabitants of agricultural areas, but also by inhabitants of towns and settlements who consume infected foods which have not been appropriately processed, for example, raw milk. Sheep's milk cheese presents a serious danger of infection with brucellosis, if it is not seasoned for 70 days before it is sold to consumers. Sour-milk products and butter are infected less frequently and less massively than raw milk.

Man may also contract the disease as a result of penetration of brucellae through fissures and excoriations in the skin and mucosa of the lips and nose. This mechanism of infection is possible in people working with livestock (milkmaids, cattle-yard workers, cattle-breeders) or helping them during abortions (veterinary workers) because numerous brucellae are eliminated together with the abortive foetus and amniotic fluid of animals infected with brucellosis. To avoid contracting brucellosis, the people attending infected animals must wear rubber gloves and boots, oilcloth aprons, special masks and coveralls.

Thus brucellosis may be contracted enterally and by various contacts of a healthy person with an infected animal. The predominant mechanism of human infection today and under definite conditions may be revealed only by consideration of all epidemiological factors.

Most authors deny the importance of brucellosis patients as sources of infection, even though they eliminate the causative agent of the disease in the urine during the febrile period. Owing to this it is necessary to hospitalize brucellosis patients, by placing them in contagious departments of hospitals.

Pathogenesis and pathologic anatomy. The pathogenesis of brucellosis may now be characterized as follows. After entering the organism of a healthy susceptible person through the mouth some brucellae disintegrate in the stomach, while others pass into the intestines and lodge themselves in their walls where they produce the primary inflammatory changes in the region of the atrium of infection. Soon the brucellae penetrate into the mesenteric and retroperitoneal lymph nodes where they multiply and cause proliferation of reticular elements. This process takes a considerable part of the incubation period. At the end of this period the brucellae invade the blood stream and give rise to bacteraemia (generalized infection). The brucellae carried by the blood flow are retained in various lymph nodes, the bone marrow, liver and spleen, where they greatly multiply and whence they re-enter the blood stream. In addition to these processes of generalization of the infection marked proliferation of reticuloendothelial elements develops in various organs and forms cellular accumulations—nodules and infectious granulomas.

As the pathologic process in brucellosis patients progresses, the infection produces general clinical and pathomorphological changes in the patient's organism as a result of the proliferation of cells of the reticuloendothelial system, affection of synovial membranes, mucous membranes of joint capsules, tendons, fasciae, intermuscular connective tissue and small blood vessels.

Endovasculitides and granulomatous processes often due to allergic states of the organism develop in small vessels. Some cases are accompanied by specific myocarditides and endocarditides, and now and then by foci of pneumonia produced by the brucellae.

Histological examination of the liver of persons who died during an early stage of the disease reveals toxic changes and, later, proliferation of reticular tissue with development of granulomas and sclerosis.

The spleen is usually enlarged; the initial stage of the disease is marked by proliferation of the reticuloendothelium with formation of granulomas and subsequent development of fibrosis of the spleen.

Brucellosis may also affect many other organs, including the central nervous system (to the point of meningoencephalitides and mental disorders), the sexual sphere and the bone marrow. But the supportive and motor apparatus—tendons, joints, ligaments and synovial membranes—is affected particularly frequently. This is characteristic of brucellic infection.

The development of functional and pathomorphologic changes in the different organs and systems is the result of secondary invasion of brucellae and of allergic reactions in the sensitized organism.

Clinical picture. The incubation period lasts 6-30 days, usually about 18 days.

The development of the clinical picture of brucellosis is in a

number of cases preceded by a prodromal period lasting from one to several days. The symptoms of this period (general indisposition, poor appetite and sleep, headache, irritability, etc.) do not particularly characterize this disease.

One of the earliest clinical signs of brucellosis is a febrile reaction. As a rule, the disease sets in gradually, but in about 15-18 per cent of the cases the onset is acute.

In most patients the temperature rises to a high level already between the 6th and 8th days of the disease and persists at that level during the days immediately following.

In brucellosis the temperature curves differ; they may be (1) undulant (usually in Malta fever caused by *Brucella melitensis*) (Fig. 59), (2) remittent, (3) intermittent, and (4) constant, with morning and evening temperature differences of 1°C.

The last type of curve is the least frequent. The temperature of brucellosis patients is usually inconstant because of the repeated passage of brucellae into the blood from the already formed foci in the tissues and because of the varying intensity of bacteraemia due to formation of new foci in the tissues.

Examined between the 7th and 9th days of the disease the brucellosis patient exhibits a discrepancy between his temperature and general condition which is still quite satisfactory. Brucellosis patients often retain their working capacity for a number of days and must take to bed only later, in connection with the progress of the disease.

This early period of brucellosis is characterized by pains in the small of the back, lumbosacral joint and muscles of the neck. No less characteristic is the recurrent and copious sweating which exhausts the patient and may be observed even at absolutely normal temperature.

During the first days of the disease the skin on the face is usually slightly hyperaemic, but subsequently all of the skin becomes pale.

During the primary generalization of the infection there is comparatively rarely any eruption, although there may be roseolas and less frequently petechiae mainly on the lower extremities. In cases of very massive invasion of brucellae there may be an abundant haemorrhagic rash on the skin. An urticarial or nodular eruption on the skin is possible in 3-4 per cent of all cases.

By the end of the second week of the disease all symptoms of brucellosis connected with the primary generalization of the infection reach their highest development and are accompanied by changes in different organs and systems.

During this period of the disease the temperature stays at a high level, the patients become very irritable and are discomforted by copious sweat and pains not only in the lumbar region, as in the first days, but also in various large joints. In some patients (approximately 25 per cent) the axillary, occipital, inguinal and other

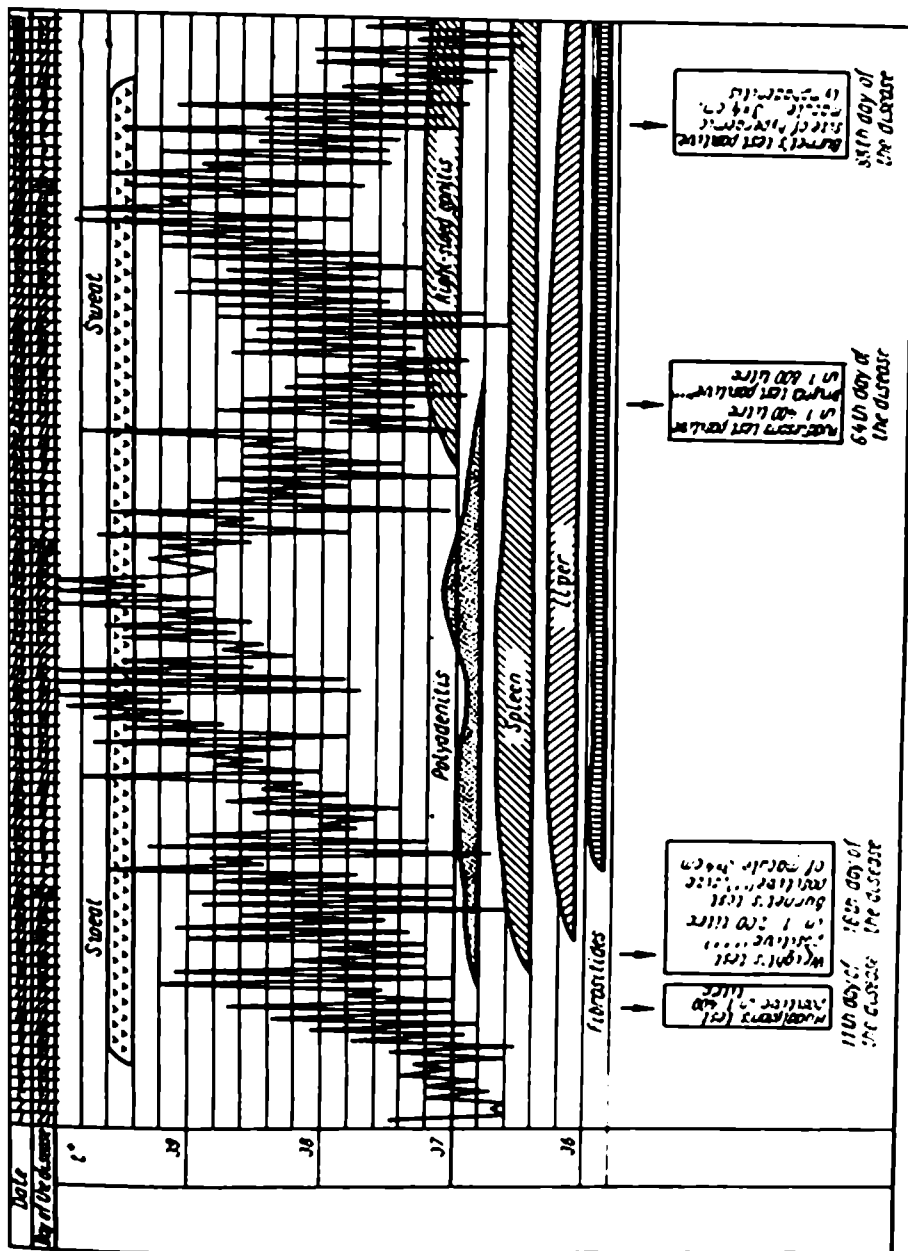


Fig. 59. Dynamics of principal clinical symptoms and diagnostic reactions in subacute brucellosis patient

peripheral lymph nodes are enlarged. They are not many, are slightly painful on palpation and do not adhere to each other or to the skin. In the acute stage of brucellosis (during the primary generalization of the infection) the liver and spleen are enlarged in 75-80 per cent of the patients.

Thorough palpation in the lumbosacral region, around the joints, on the thighs, along the ribs, above and below the clavicles, and in the region of the wrist often reveals small compact nodules and indurations of connective tissue—*fibrositides* and *cellulitides* (usually observed in subchronic and chronic forms of the disease). The pulse rate usually corresponds to the level of the temperature, the blood pressure is slightly lowered. Some patients develop endo- and myocarditides. Specific brucellic vasculitides accompanied by a certain paresis of small blood vessels and increased permeability of the capillaries are observed in a large number of all cases of acute, subacute and chronic brucellosis. Myocardial dystrophy (moderate extension of the borders of the heart, dull sounds and systolic murmur at the apex with corresponding changes in the electrocardiogram) may be observed in one-third of all brucellosis patients. Owing to the inflammatory allergic changes in the small blood vessels (brucellic vasculitis) and increased permeability of the vascular wall, tissue respiration and normal processes of tissue nutrition are disturbed. Simultaneously the disorders of water-salt, carbohydrate and protein metabolism increase. The hepatic functions are moderately disturbed.

The clinical symptomatology of affections of the nervous system is very diverse and ranges from moderate neuralgias and neuritides of separate nerve trunks to severe meningoencephalitides, encephalitides and profound mental affections.

Brucellosis affects the haematopoietic functions of the bone marrow. The changes in cellular composition of specimens of bone marrow obtained by puncture are due primarily to the presence of actively multiplying brucellae in it. The picture of peripheral blood is characterized by leucopenia, relative (in per cent) lymphocytosis, neutropenia with a moderate shift to the left and eosinopenia. The ESR is accelerated (up to 25-40 mm/hr), thrombocytopenia is observed, and in cases of subchronic and chronic brucellosis moderate hypochromic anaemia is possible. Pregnant women affected with brucellosis may have an abortion.

Symptoms on the part of the joints (Fig. 60) and the entire supportive and motor apparatus serve as some of the most characteristic manifestations of brucellosis in the stage of local affections. It may be said without any exaggeration that the joints, tendons and bursae are in some measure affected in almost every patient (arthritides, tendovaginitides, bursitides—Fig. 61). Usually the *large* joints are affected (sacrocoxitides, spondylitides, coxitides, gonitides); development of osteoperiostitis with destruction of bony

tissue is possible. The ankle and shoulder joints are affected somewhat less frequently.

In acute brucellosis the affection of joints is usually manifested in sharp pains, while in subchronic and chronic brucellosis the joints are oedematous, enlarged and even less movable. In addition to the affection of joints, subchronic (subacute) and chronic brucellosis exhibits inflammatory changes in the tissues surrounding the



Fig. 60. Brucellic arthritis of right shoulder joint

joints (periarthritides). Protracted and stable affection of joints results in contractures and ankyloses. As a rule, only 1 or 2 joints are affected at each given moment, i.e., there is no shifting of the joint affection. In these cases the large joints are affected and not the small ones as in rheumatic polyarthritis. Tendovaginitides and bursitides are often observed (Fig. 61).

After termination of the initial generalization the temperature drops to normal, the patient's condition improves, and the disease may enter the phase of protracted latency. However, this does not exclude the possibility of recurrent relapses and generalization of the infection, including intense bacteraemia in cases of subchronic and chronic brucellosis.

The period of acute brucellosis (phase of generalization of the infection) lasts from 2-3 weeks to 3 months. The most important symptoms of this period of the disease are chills, high temperature, recurrent sweating, enlargement of the liver and spleen (hepatolienal syndrome), pains in the lumbosacral region and, in some

patients, peripheral lymphadenitides with predominant enlargement of the axillary, occipital and ulnar lymph nodes. The blood picture is characterized by leucopenia with relative lymphocytosis, aneosinophilia and neutropenia. The spleen is enlarged in 75-80 per cent of all patients in this stage of the disease.

In subchronic brucellosis (otherwise designated as the phase of localization of the infection with relapsing generalization), in addition to many symptoms characteristic of the acute form of the disease and the febrile reaction, there are numerous local affections,



Fig. 61. Brucellic bursitis of left knee joint

usually of the supportive and motor system (joints, tendons, ligaments and bursae), and of the peripheral nervous system (neuritis, neuralgias, etc.). Manifestations of haemorrhagic diathesis (nose-bleed, and in women - uterine haemorrhages) are not infrequent. The liver and spleen long remain enlarged. This stage of the disease lasts 2-3 months.

Chronic brucellosis is accompanied by stable changes in joints with development of contractures and ankyloses and frequently by changes in the nervous system (neuralgias and neuritis); the liver and spleen are enlarged and indurated. Chronic brucellosis may last 3-5 years and even longer, and is followed by compensation of the pathologic process and recovery; however, the severe affections of the joints and spine may lead to invalidism.

Complications. The most typical complications of brucellosis are orchitis and epididymitis, salpingo-oophoritis and oophoritis, pneumoniae, and stable and irreversible changes in the large joints and spine, including spondylitis, permanent contractures and

ankyloses. Some cases are accompanied by protracted lumbar ischialgias and radiculitides which resist treatment.

Brucellosis is accompanied by formation of immunity which does not, however, attain considerable development since the causative agent is long retained in the organism and the disease often runs a protracted and even chronic course; re-infection and relapses are possible.

Diagnosis. Brucellosis is diagnosed on the basis of a careful revealment of the epidemiological data, especially if the patient lived for 2-4 weeks before the onset of the disease in the area where there is an epizootic of brucellosis; due consideration is also given to all clinical and laboratory data.

During the first 8-10 days the disease should be *differentiated* from typhoid fever, malaria, miliary tuberculosis, focal pneumonia, subacute septic endocarditis and septic diseases of various aetiology.

The moment symptoms of affection of the supportive and motor apparatus appear it is necessary to differentiate the disease from infectious (deforming) and rheumatic polyarthritis. It should be remembered that the latter is characterized by affection mainly of small joints, shifting pains with acute inflammatory changes simultaneously in many joints, namely, considerable oedema of the periarticular tissue, effaced joint contours, hyperaemia of the skin covering the joints, limited and painful movements in the affected joints.

The laboratory diagnostic methods used are serological tests (Wright's and Huddleson's tests) and Burnet's allergic skin test.

Wright's test is conducted in test-tubes with the serum of the patient's blood diluted with physiologic solution (1 : 50, 1 : 100, 1 : 200, 1 : 400 and 1 : 800); 1-2 drops of a killed culture of brucellae are added to each test-tube and the latter are placed in a thermostat for 20-24 hours at 37°C.

A positive Wright's test in a 1 : 200 dilution of the serum and higher should be considered a demonstrative diagnostic titre. Repetitions of this test at later periods show an increase in its titres, although they never reach very high figures. In a number of cases Wright's test may be positive already on the 8th or 9th day of the disease in lower titres, but it usually becomes positive in diagnostic titres only on the 10th or 11th day.

For practical purposes Huddleson's test is simpler and more convenient; it may be conducted right at the patient's bedside. It should be remembered, however, that, while this test is sensitive enough, it may produce nonspecific results.

For Huddleson's test about 1 ml of blood is taken from the patient's finger; the settled serum must be absolutely transparent. A plate of window glass thoroughly degreased by alcohol and divided into six squares is used. The patient's blood serum is poured into each square by means of a graded pipette in the following

amounts: 0.08, 0.04, 0.02 and 0.01 ml. One drop of Huddleson's antigen (killed culture of brucellae stained with methylene blue) is added to each dose of the serum, after which the serum, beginning with the minimum dose, is carefully mixed with the antigen by means of a glass rod. The control of the agglutinating properties of the serum is tested in the fifth square (0.03 ml of serum and 0.03 ml of physiologic solution) and the control of the antigen (0.03 ml of antigen and 0.03 ml of physiologic solution) — in the sixth square. Then the glass is evenly heated for 2 minutes over the flame of an alcohol burner. If the test is positive, flakes stained blue (agglutination) appear within 6-8 minutes in the drops of serum to which the killed culture was added.

Wright's and Huddleson's tests, as well as Burnet's test (see below), may remain positive long after the attack of brucellosis (sometimes for several years). In order to draw a competent conclusion as to whether the disease is in an active stage in cases of chronic brucellosis it is therefore necessary to compare all the clinical data with the indices of the afore-said tests.

For Burnet's allergic skin test (see Fig. 5) melitin (brucellin) is used; it is a filtrate of a broth culture of brucellae containing the antigenic substances of these bacteria.

By means of a 1-g syringe with a thin needle 0.1 ml of melitin is administered into the skin of the forearm. The results of the test may be read 24 hours after its performance. Twenty-four hours after administration of brucellin the patient develops a hyperaemic macule on the skin, oedema of soft tissues with infiltration along the edges of the hyperaemic part, and sometimes lymphangitis with a swelling of the regional (axillary) lymph node. A hyperaemic zone of the skin measuring at least 3.5×3 cm is regarded as a diagnostic sign.

Prognosis. With a timely diagnosis and vigorous treatment the prognosis is almost always favourable. But in cases of so serious a complication as acute or subacute brucellic endocarditis the disease becomes very dangerous to life.

In a number of cases where brucellosis runs its usual course it causes irreversible changes in the large joints with resultant permanent contractures and ankyloses; particularly severe are the results of sacrocoxitis or affections of the spine requiring surgical intervention.

Treatment. All brucellosis patients must be hospitalized during the acute (generalized) period, in cases of a subacute course of the disease and aggravations of chronic brucellosis.

These patients must be ensured the maximum of care and attention by the attending personnel because brucellosis patients are emotionally very labile: irritable and often given to crying (usually women). The protracted course of the disease, pains in the joints and peripheral nerves, frequent complications and not always effec-

tive treatment are the cause of all these peculiarities of the patients' neuropsychic sphere and call for psychotherapy (sympathetic talks with the patients) and favourable conditions in the wards of brucellosis patients (hygienic atmosphere, proper diet and particularly good care).

Brucellosis patients must be given a varied diet containing adequate proteins, fats, carbohydrates, mineral salts, vitamins and sufficient calories.

During the period of hospitalization (i.e., during the entire first acute period of the disease and during the recurrent phases of generalization of the infection in cases of subacute and chronic brucellosis) treatment with antibiotics (synthomycin, levomycetin, biomyacin, tetracycline) is indicated.

Levomycetin is administered in the following doses: 0.5 g 6 times per day until normalization of the temperature and for 3 days thereafter, then 0.5 g 4 times per day for 8-12 more days.

Synthomycin is administered in similar doses.

These antibiotics quickly lower the temperature, mitigate the changes in the liver and spleen, and diminish the focal affections (of the supportive and motor apparatus, the peripheral nervous system, etc.). However, this is only a temporary abatement of the pathologic symptoms (remission), and it is therefore advisable to give the patient (15-25 days after the end of the first course) another course of treatment with the same antibiotic (for example, 0.5 g of levomycetin 6 times per day for 8-10 days), which considerably diminishes the possibility of relapses and the transition of the disease to subacute and chronic forms.

Tetracyclines have certain advantages in the treatment of brucellosis. Biomyacin is administered in a dose of 300,000 U 4 times per day until normalization of the temperature and for 2 more days, after which it is administered in smaller doses (200,000 U 4 times per day for 8-12 days). Treatment with biomyacin leads to rapid normalization of temperature; it is *more effective* than treatment with synthomycin and levomycetin. Tetracycline which is administered in the same doses as biomyacin is also very effective.

The patient may discontinue taking the antibiotics only 10 days after normalization of the temperature.

It should be remembered that it is necessary to start administration of antibiotics as early as possible.

Since treatment with antibiotics alone is insufficient to produce a *complete* and *stable* therapeutic effect in a number of cases, vaccine therapy with polyvalent therapeutic vaccines of killed cultures of brucellae is being widely used mainly in cases of *subacute* and *chronic* brucellosis.

The vaccine diluted with physiologic solution may be administered in three ways: intracutaneously, subcutaneously and intravenously.

If the first method is used, the vaccine is administered strictly intracutaneously into the forearm or thigh in a dose of 0.1 ml in several places in accordance with the total dose of the vaccine. In the first injection the patient receives 25,000,000 microbial bodies; every two days the number of injection sites is increased so that in the 8th injection a total of 400,000,000 microbial bodies is administered, the dose being divided into 16 parts, each part being injected into a different portion of the skin. This method produces favourable direct results when combined with administration of antibiotics (biomycin, tetracycline).

According to the subcutaneous method which is very rarely used today, the patient is subcutaneously administered the therapeutic vaccine in increasing doses at 3-day intervals; the dose of 15,000,000 microbial bodies at the first administration is increased to 1,000,000,000 microbial bodies at the end of the course consisting of ten injections. This method is less effective than the intracutaneous method.

The intravenous method of vaccine therapy is the most effective, especially when combined with the patient's intake of biomycin which, like tetracycline, is prescribed in a dose of 300,000 U 4 times per day.

Before administering intravenous vaccine therapy it is necessary to test the patient's sensitivity to the vaccine. For this purpose 500,000 microbial bodies are administered at first. The usual post-vaccination reaction manifests itself in mild chills, rise in temperature, general indisposition and intensified pains in the organs of the supportive and motor system; this is a very favourable reaction for it warrants the assumption that the course of vaccine therapy will be productive of good effects. Sometimes, however, the patient reacts with a severe shock owing to which vaccine therapy has to be rejected.

Intravenous vaccine therapy consists in administration of 1,000,000, 3,000,000, 5,000,000, 10,000,000, 25,000,000, 50,000,000 and 75,000,000 microbial bodies per injection at 3-4-day intervals (a total of 8-10 injections).

To minimize the possibility of undesirable shock phenomena, *two-stage vaccine therapy* is administered by G. P. Rudnev's method. The daily dose of the vaccine is divided into two intravenous injections with an interval of 1.5-2 hours. The doses of vaccine used in this method are smaller than in the foregoing method.

In the first (preparatory) administration the patient receives 200,000 microbial bodies and in the second (resolving) administration—250,000 microbial bodies; 3-4 days later 300,000 and 300,000 microbial bodies are administered and after another 3-4 days 400,000 and 400,000 microbial bodies are injected (the first figure is the dose of the "preparatory" administration, the second figure—the dose of the "resolving" administration). The doses are increased

at each successive administration (with the same intervals) so that in the last injection the patient is administered 2,000,000 and 2,000,000 microbial bodies.

To stimulate the defensive factors of the organism, the patients are given blood transfusions of 125-150 ml of blood of the same group or of the 1(0) group at 3-4-day intervals (a total of 4-5 transfusions).

Soon after abatement of the pathologic process in the joints it is necessary to give the patient kinesitherapy, paraffin or ozocerite applications and a number of other physiotherapeutic procedures which help to restore active movements and muscle tone.

Subsequently, in the absence of any acute manifestations of brucellosis and when the ESR has slowed down to 16-18 mm/hr or even to lower figures, the convalescent may be referred to a health resort for pelotherapy and mineral-water treatment.

Prevention. The most important measures for preventing brucellosis in the foci of this infection are thorough veterinary inspection of livestock, isolation of infected animals on special brucellotic farms, and protection of the people working on these farms: the protection consists in wearing rubber gloves, oversleeves and rubber boots while looking after the animals or helping them during spontaneous abortions.

Depending on the concrete routes of transmission of the infection brucellosis may be of an alimentary or occupational character. However, the enteral (alimentary) route of transmission of the infection is the most important in the epidemiology of brucellosis, and this must particularly be taken into account in the organization of a system of preventive measures.

Regardless of whether the people have any direct connection with animals infected with brucellosis everybody, especially in areas where this disease occurs, must consume only boiled or pasteurized (heated twice to 70°C) milk.

All dairy products must be made only from pasteurized milk; sheep's milk cheese must be seasoned for 70 days before consumption.

Meat obtained from animals infected with brucellosis may be canned only by autoclaving; in some cases the meat of animals infected with brucellosis may be consumed after long (for 3 hours) cooking in small pieces at 100 C.

People working on farms with brucellotic animals must keep the skin of their hands and feet thoroughly clean and intact because the infection may penetrate into the organism even through the slightest abrasions, scratches and cracks in the skin.

The manure of infected animals must be disinfected with composts; the buildings for animals on brucellotic farms must be systematically disinfected; the floor and dungwash receivers must be repeatedly flooded with a 10 per cent calcium chloride solution; the walls must be sprayed with the same solution.

The abortive fetuses of animals infected with brucellosis must be buried deep in the earth (the grave must be at least 2 m deep and its floor must be covered with a heavy layer of quicklime). The building where a brucellic animal has brought forth its young must be disinfected with a 10 per cent clarified calcium chloride solution.

An auxiliary role in the prevention of brucellosis is played by inoculations with a vaccine of a living vaccine strain of *Brucella abortus*. This method elaborated by Soviet authors fosters a certain decrease in brucellosis incidence among immunized people. Directly before vaccination the living dry brucella vaccine is dissolved in sterile physiologic solution and administered subcutaneously in one immunizing dose. The inoculation ensures relative immunity for about 1 year.

ICTEROHAEMORRHAGIC LEPTOSPIROSIS OR WEIL-VASILYEV'S DISEASE (MORBUS WEIL-VASILYEV, LEPTOSPIROSIS ICTERO-HAEMORRHAGIAE)

Icterohaemorrhagic leptospirosis, caused by a special strain of leptospirae (*Leptospira ictero-haemorrhagiae*) is an acute infectious disease accompanied by a febrile reaction, affection of the parenchyma of the liver with development of jaundice, numerous haemorrhages in the skin, on the conjunctivae and the mucous membranes, and by symptoms of diffuse haemorrhagic nephritis.

Brief historical information. In 1886 A. Weil described in Germany 4 cases of a disease accompanied by jaundice, enlarged spleen and nephritis, and mistook this disease for an atypical form of typhoid fever. In 1888 N. P. Vasilyev, pupil and associate of the outstanding Russian clinician S. P. Botkin, established the nosological entity of the disease on the basis of clinico-anatomic parallels.

Thanks to N. P. Vasilyev the disease was given quite a full description in all its main clinical manifestations.

In 1914 the Japanese scientists Inada and Ido and their associates discovered the causative agent of the disease—the icterohaemorrhagic leptospire (*Leptospira ictero-haemorrhagiae*).

Later new data were accumulated concerning the clinical aspects, epidemiology and pathologic histology of the disease, the causative agent was studied and problems of experimental leptospiral infection were elaborated. A substantial contribution to elaboration of the problems of icterohaemorrhagic leptospirosis was made by Soviet scientists V. I. Torsikh, K. N. Tokarevich, A. A. Varfolomeyeva, I. I. Nikolayev, V. S. Kiktenko, and others.

Aetiology. The causative agent of icterohaemorrhagic leptospirosis is the icterohaemorrhagic leptospire. The leptospire is about 10-16 μ long and 0.25 μ thick. Its body consists of several spirals; its ends are hooked. The leptospire performs active translational movements and sideward bends; its hooked ends make vigorous rotatory movements. The microorganism multiplies by direct division.

The leptospire may be cultivated in artificial nutrient media (optimum growth at pH= 7.2 and temperature of 28-29°C). The usual medium consists of tap water (100 ml), defibrinated rabbit blood (2 ml) and agar (0.2 g). The medium is poured into sterile test-tubes and is sterilized in an autoclave. The leptospires multiply slowly, over a number of days. After 5-6 days of incubation in a thermostat it is advisable to transfer the culture to other test-tubes with the same medium.

In a pure culture or in biological substrates leptospires may be discovered under the microscope in specially stained preparations; for this purpose the preparations are preliminarily fixed in a mixture of alcohol and ether (1 : 1) and then stained by diluted Romanovsky-Giemsa dye (1 ml of the dye per 50 ml of distilled water) for 6-8 hours.

Epidemiology. Various rodents, rats in particular, are the reservoir of the infection in nature. In the organism of the infection carriers leptospires are present mainly in the lumens of the convoluted tubules of the kidneys; they are eliminated into the external environment in the animals' urine. This may contaminate the soil, foodstuffs and water (closed reservoirs—wells, lakes and ponds). Humans become most commonly infected through consumption of contaminated water and foodstuffs and through bathing because the water is often contaminated with the urine of rats, and leptospires may penetrate into the organism through damaged skin.

The seasonal incidence (August-September) of icterohaemorrhagic leptospirosis is due to the fact that at this time of the year leptospires are better preserved, the number of rats increases, people go swimming and engage in agricultural work. It should be remembered, however, that cases of this disease may also be observed all-year-round, especially among people doing earthwork.

Icterohaemorrhagic leptospirosis occurs in countries with a tropical and subtropical climate (including Japan, Indonesia and India); in Europe the disease is observed mainly in Holland and Belgium because these countries have an extensive canal system (water route of infection).

On the territory of the USSR only single cases of icterohaemorrhagic leptospirosis are now observed.

Pathogenesis and pathologic anatomy. Leptospires gain entrance into the human organism mainly through damaged skin and through the mucous membranes of the mouth and the digestive tract.

After generalization of the infection which takes place during the incubation period of the disease the leptospires lodge themselves in different human organs and tissues, mainly the kidneys, liver, spleen, lymph nodes and bone marrow; on the 7th or 8th day of the disease leptospires begin to be eliminated in the urine.

Histological examination of the tissues and organs of people who have died of icterohaemorrhagic leptospirosis reveals marked changes

in the liver and kidneys with resultant jaundice and haemorrhagic nephritis and symptoms of nephrosis. The affection of the liver, the jaundice and disrupted continuity of the endothelium of capillaries (diapedetic bleeding) result in numerous haemorrhages in the skin and mucous membranes.

The skin and mucous membranes are extremely icteric; there are petechial haemorrhages in the skin, mucous and serous membranes, and the adrenals. The tissue of the liver also contains numerous petechial haemorrhages; the liver is yellow and compact; histological examination shows parenchymatous and fatty degeneration of hepatic cells. The spleen exhibits numerous focal haemorrhages. Microscopic examination of the kidneys reveals a picture of haemorrhagic nephritis with simultaneous affection of the uriniferous tubules. There are numerous haemorrhages in the dura.

An attack of the disease confers lasting immunity.

Clinical picture. The incubation period is 4-13 days (it averages 6-8 days). The disease sets in acutely with chills and a sharp rise in temperature which reaches 39.5-41°C in the first 24 hours. The main complaints of the patients are headaches and particularly sharp pains in the gastrocnemius muscles. The patient's face is hyperaemic; some cases are accompanied by conjunctivitis; the gastrocnemius muscles are painful to touch.

During the very first two days of the disease the tongue becomes dry and coated with a yellowish-brown film; the abdomen is usually inflated; the liver becomes enlarged, compact and painful. The spleen enlarges from the 3rd or 4th day of the disease; the mucosa of the hard palate, the sclerae (Fig. 62) and all of the skin become icteric at the same time. The period of development of jaundice coincides with the stepped fall of the temperature which becomes normal on the 8th or 9th day of the disease.

The pulse rate usually lags behind the temperature level (relative bradycardia). The patient's output of urine is decreased and the urine contains erythrocytes, protein (up to 3 per cent), hyaline and granular casts. The blood picture is characterized by moderate leucocytosis (9,000-10,000 leucocytes per 1 cu mm). The reaction to bilirubin in the blood is direct, quick and sharp.

The period of convalescence begins on the 10th or 11th day of the disease; the pains in the gastrocnemius muscles cease, the jaundice becomes milder and the urine normal. The disease lasts a total of about 3 weeks.

Some patients may have relapses; in these cases the temperature rises again 5-7 days after the end of the first attack and the second febrile attack lasting 4-5 days begins.

During relapses the clinical picture of the disease is quite characteristic, but the blood shows considerable leucocytosis and the patient is more markedly anaemic. The second febrile period is fol-

lowed by slow recovery with a gradual restoration of the patient's strength.

Complications. Most typical signs of haemorrhagic diathesis are severe haematurias, bloody vomiting, haemorrhages from mucous membranes, and otitides, parotitides and muscular atrophy; individual cases may be accompanied by severe myocarditis; the disease may also become aggravated by leptospiral meningitis.

Prognosis. If treatment is begun early and is administered vigorously, favourable results may be expected. Only if the disease runs a particularly severe clinical course may the prognosis be very serious, as it may also be in cases of aggravation of the disease by myocarditis, otitis and haemorrhagic nephritis. An attack of the disease confers lasting immunity.

Diagnosis. Icterohaemorrhagic leptospirosis is diagnosed on the basis of epidemiological data and the clinical picture. It is necessary to take into account the acute onset of the disease with chills and the rapid and considerable rise in the temperature, development of jaundice, enlargement of the liver, appearance of haemorrhages on the skin and mucous membranes, sharp muscular pains and symptoms of haemorrhagic nephritis.

Differential diagnosis. The disease must be differentiated from relapsing fever, anicteric leptospirosis and Botkin's disease

Relapsing fever is characterized by a constant and early enlargement of the spleen, tachycardia, neutrophilic leucocytosis and thrombocytopenia of the blood; the kidneys are unaffected; an important role is played by discovery of the *Spirochaeta obermeieri* in a thick stained drop.

Anicteric leptospirosis is accompanied by appearance of a polymorphous eruption on the skin and a critical fall of the temperature on the 7th day of the disease; the liver is not enlarged and is painless; jaundice is observed only in single cases and haemorrhages in the skin are rare.

Botkin's disease which is caused by a filtrable virus is characterized by a gradual onset with a pre-icteric period (dyspeptic phenomena, early enlargement and painfulness of the liver, presence of bile pigments in the urine), absence of muscular pains, slight or total absence of any changes in the kidneys. During the icteric period of Botkin's disease the stool is discoloured for several days; this period is marked by leucopenia and relative lymphocytosis of the peripheral blood.

Several laboratory methods are used in diagnosing icterohaemorrhagic leptospirosis.

Leptospire may be discovered during the febrile period of the disease in a drop of the patient's blood plasma by microscopy under dark field illumination. For this purpose the plasma is at first enriched, i.e., 3 ml of the patient's blood is mixed with 2 ml of a 2 per cent sodium citrate solution and is centrifuged at 1,500 r min

for 6 minutes; the upper layer is drawn off and centrifuged again under the same conditions; a drop of the plasma taken from the bottom of the test-tube is examined under the microscope (in a dark field with side illumination by means of a special illuminator).

By inoculating the blood (during the first 4-5 days of the disease) and urine (from the 6-7th day of the disease) in a medium consisting of tap water, defibrinated rabbit blood and agar it is possible to isolate leptospire. The incubation of the culture must take place in a thermostat at 28°C. Microscopy of the culture under dark field illumination after 7-8 days of its growth reveals leptospire.

It has been demonstrated that the patients' blood serum agglutinates leptospire and causes lysis. This circumstance is used for an agglutination-lysis test in test-tubes or on a slide; the test may be performed only with a living strain of leptospire because no killed culture of these microbes has as yet been obtained, owing to which it is difficult to perform the agglutination-lysis test for leptospire in hospitals. The test is performed only in special laboratories where several drops of the patient's blood serum dried on a sheet of filter paper may be sent. The agglutination-lysis test is highly specific and sensitive.

The laboratory methods of diagnosis include infection of the guinea pig by intraperitoneal administration of 5 ml of the patient's fresh blood; leptospire may be discovered in the exudate of the guinea pig's abdominal cavity as soon as 3 days after the infection.

Treatment. Icterohaemorrhagic leptospirosis patients must be hospitalized and kept strictly in bed. The patient's general condition, renal functions, state of the liver and haemorrhagic manifestations need careful watching. The patients are prescribed a diet of semiliquid, easily assimilable food consisting mainly of carbohydrates; dairy products—varieties of soured milk and, especially, curds which favourably influence the functional state of the kidneys—are recommended.

In cases of marked changes in the kidneys the patients are prescribed a corresponding dairy and vegetable diet with limited consumption of sodium chloride. The patients must be administered a 40 per cent glucose solution (intravenously 50 ml per day) every day all through the febrile period.

Treatment with penicillin is effective; this antibiotic must be administered intramuscularly in a dose of 400,000 U 3 times per day until normalization of the temperature and then in somewhat smaller doses (300,000 U 3 times per day) for 3 more days.

Prevention. The main measures in the prevention of icterohaemorrhagic leptospirosis are extermination of rats by mechanical, physical and chemical methods, and thorough protection of wells and surface water reservoirs against their possible contamination with the urine of rats which are the carriers of pathogenic leptospire. Consumption of only boiled water reliably prevents water-

borne infection with leptospirosis. In rivers and lakes it is necessary to bathe near the higher bank or shore where the water is difficult of access to rats.

If a collective or the population of a community is in danger of becoming infected with icterohaemorrhagic leptospirosis, it must be instructed in sanitation and hygiene and acquainted with the main routes of transmission of the infection. Vaccination plays an auxiliary role.

In areas where there are cases of icterohaemorrhagic leptospirosis it is necessary to carry out meliorative work—drying and draining of swampy terrain. People engaged in agricultural work, mining and earthwork must wear special working clothes and footwear in order to prevent penetration of leptospires to damaged skin.

MARSH FEVER OR ANICTERIC LEPTOSPIROSIS

Marsh fever or anicteric leptospirosis is an acute infectious disease transmitted to man by rodents through water contaminated with their urine, and by pigs which are carriers of the infection; the disease is characterized by a febrile reaction, hyperaemia of the face, conjunctivitis and eruptions on the skin; relapses of the disease are possible.

Brief historical information. The disease was first observed during a water epidemic of marsh fever in Silesia in 1887. In 1927-1928 V. A. Bashennin, V. I. Terskikh and S. I. Tarasov made a detailed study (on the territory of the USSR) of the epidemiological characteristics and clinical aspects of the disease; they also isolated its causative agent. A. A. Varfolomeyeva and her associates conducted a number of interesting investigations.

Aetiology. Two types of marsh fever are distinguished in accordance with their causative agents: type I caused by the *Leptospira grippotyphosa* and type II caused by the *Leptospira monovalens*.

Morphologically these leptospires are very similar and are distinguished by their antigenic patterns. The causative agents are actively motile and may be cultivated in special media.

Epidemiology. Mouselike rodents which are chronic carriers of the infection are the main reservoir of type I marsh fever; cattle serve as an additional reservoir of the infection.

The infection caused by type I leptospires is transmitted through water of closed reservoirs (marshes, lakes, ponds and wells) contaminated with the urine of mouselike rodents and cattle—the carriers of the infection. The causative agent gains entrance into the human organism through the digestive tract, mucous membranes of the lips, mouth and nose, and scratches, abrasions and cracks in the skin. Humans may contract type I marsh fever by consuming raw infected water, bathing or doing agricultural work, for example, haymaking in moist, marshy areas. In the latter case leptospires penetrate into the organism through cracks in the skin of the legs.

Type II marsh fever is transmitted to humans mainly by grey

rats whose urine contains numerous leptospire. Hogs play the role of an additional reservoir of the infection; in some cases hogs carry leptospire for long periods of time. The infection is transmitted to man mainly through water (contaminated by grey rats and hogs) and also through contact (predominantly while tending hogs or through the urine of infected rats).

In addition to sporadic cases there may also be epidemics of this disease.

Pathogenesis and pathologic anatomy. The leptospire gain entrance into the human organism through the digestive tract, the mucous membrane of the lips or mouth, or through damaged skin and towards the end of the incubation period begin to circulate in the blood. From 5 to 8 days after the onset of the disease they penetrate into the internal organs (the spleen, liver and kidneys) where they give rise to moderate phenomena of degeneration. Since mortality from this disease is negligible no adequate studies of its pathologic anatomy have as yet been made.

Clinical picture. The disease sets in with intense chills followed by a rapid rise in temperature to 39-39.5°C (Fig. 63). The temperature persists at high figures for 6-8 days and then falls to normal by an accelerated lysis. Sometimes a temporary (1-2 days) relapse is possible 3-4 days after normalization of the temperature.

On the second day of the febrile period the patient assumes a typical appearance: his face and sclerae are hyperaemic and his eyes are lustrous; he develops conjunctivitis and frequent nasal haemorrhages. Patients usually complain of general weakness, headaches and muscular pains; pains in the small of the back are possible.

Between the 4th and 6th days of the disease an eruption breaks out on the skin of the chest and abdomen in 20-25 per cent of the cases; the eruption persists for 1-3 days. Sixty-five per cent of the eruptions are maculopapular, 15 per cent—roseolopetechial, and 20 per cent—petechial. Hyperaemia of the fauces is often observed; the tongue is evenly coated. The pulse rate corresponds to the temperature level. Herpetic eruptions often appear on the lips and wings of the nose.

As a rule, the liver is slightly enlarged; in some cases an enlargement of the spleen is observed. A urinalysis reveals temporary and moderate albuminuria.

Usually no jaundice is observed, but sometimes this symptom is possible; in such cases the disease should be differentiated from icterohaemorrhagic leptospirosis.

During the first four days of the disease the blood shows leucocytosis (12,000-15,000 leucocytes per 1 cu mm) with neutrophilia and a nuclear shift to the left. The urine contains traces of protein. As a rule, the disease runs a favourable course and ends in complete recovery.

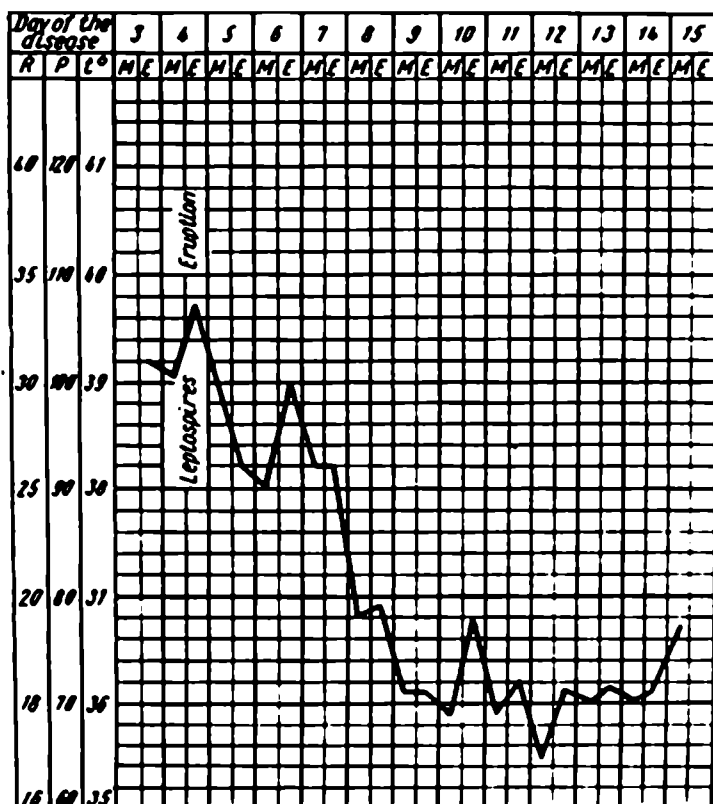


Fig. 63. Temperature curve in patient from whom the *L. pomona* strain was isolated. Type II leptospirosis

Now and then marsh fever may become aggravated by iridocyclitis or serous meningitis.

Cases of atypical marsh fever are accompanied by a subicterus of the skin and sclerae and an irregular type temperature curve with elevated temperature lasting 6-12 days.

Diagnosis. The disease is diagnosed on the basis of its clinical picture and consideration of the epidemiological data; laboratory methods of diagnosis play an auxiliary role.

The blood of patients contains agglutinins, lysins and complement fixation antibodies, which are used for laboratory diagnosis of the disease.

As a rule, antibodies are found in the patient's blood serum for 3-4 days beginning with the 5th or 6th day of the disease; their titre increases and reaches its maximum between the 14th and 16th days of the disease with a subsequent stabilization for 1-2 weeks or slight decrease. After a month of the disease the titre de-

creases to 1 : 100-1 : 200; these figures may persist for several months, which is of some importance for retrospective diagnosis.

A highly specific agglutination-lysis test is the most generally used laboratory method of diagnosis; this test should be performed dynamically from the 4th or 5th day of the disease.

Differential diagnosis. The disease must be differentiated from influenza, typhus (see Table 5), icterohaemorrhagic leptospirosis, malaria, Q fever and in corresponding endemic areas also from papataci fever.

Prognosis. The disease runs a favourable course and with timely treatment ends safely; the health and working capacity of the patients are quickly restored.

Treatment. All patients must be hospitalized. Intramuscular administration of massive doses of penicillin (1,200,000-1,500,000 U per day) is an effective method of treatment; the dose is divided into 3 portions dissolved in 1 ml of 0.5 per cent of novocain. The course of treatment is 5-6 days.

Prevention. Consumption of raw water from closed reservoirs (lakes, ponds, marshes) must be absolutely prohibited. While working in marshy areas, for example, haymaking, it is necessary to wear rubber boots and gloves. Bathing in small closed reservoirs must also be prohibited. Grey rats and mouselike rodents must be exterminated. People working on hog farms must exercise caution; it is necessary to reveal the infected animals. Piggens must be systematically disinfected and the rats in them must be exterminated because rats may transmit the infection from the hogs. Rats are exterminated with bait containing zinc phosphide.

A method of specific vaccination with a suspension of leptospirae inactivated by heating (Varfolomeyeva-Kovarsky's vaccine) has been developed in recent years. The vaccine is administered subcutaneously in a dose of 2 ml twice, with an interval of 7 days; immunity develops 15-20 days after the second inoculation and lasts one year.

GLANDERS (MALLEUS)

Glanders is a general infectious human disease of zoonotic origin and is characterized by formation of granulomas, pustules and abscesses in various tissues and organs; it occurs in an acute and a chronic forms.

Brief historical information. The disease has been known since antiquity.

In the 1840-s it was demonstrated that the disease is caused in humans and animals by the same "infectious matter".

The bacteria of glanders were discovered in horses by Loeffler and Schütz in 1882 and then in a person affected with acute glanders (in the blood and discharge from the nose) by N. P. Vasilyev (in 1883).

An allergic diagnosis of glanders by the method of mallein tests was developed by C. I. Gelman and O. Kalning in 1891.

The glanders incidence was quite high even as late as last century; it usually increased at times of war (epizootics among horses). Today the disease is rare.

Aetiology. The causative agent (*Bacillus mallei* or *Malleomyces mallei*, also known as the Loeffler-Schütz-Vasilyev bacterium) is a nonmotile, gram-negative rod 2-4 μ long and about 0.6 μ thick.

Epidemiology. Livestock, especially horses, are the reservoir of infection in nature and the most important source of human infection; some role in the epidemiology of glanders is also played by diseased humans (discharge from the nose, skin pustules, muscle abscesses and, in the pulmonary form of the disease, sputum).

The causative agent of glanders may gain entrance into the organism through damaged skin and mucous membranes. Man may also become infected with the contents of pustules through the air or dust, which is favoured by respiratory catarrh in susceptible people.

Pathogenesis. Soon after gaining entrance into the human organism through the skin or mucous membranes the glanders bacteria begin to circulate in the blood, owing to which the disease assumes a septic course. Specific nodules (granulomas) form on the skin and mucous membranes; subsequently these granulomas suppurate and form ulcers. Disintegration of the nodules in the internal organs and, especially, in the muscles leads to formation of deep abscesses, most commonly in the gastrocnemius muscles. In chronic forms of glanders specific granulomas form mainly in the lungs.

Studies of the fine structure of glanders nodules in the lungs have shown that granulomas are the result of fibrinous and inflammatory changes in pulmonary tissue which undergoes caseous degeneration in the centre of the nodules with development of connective tissue on their periphery. In humans glanders is often characterized by symptoms of acute sepsis and ends lethally.

In chronic cases general intoxication of the patients and their gradual emaciation are clearly marked.

Clinical picture. The incubation period of glanders averages 4-5 days. In *acute forms* of the disease a plaque forms in the region of the atrium of infection and soon develops into a nodule or a pustule. Owing to the penetration of the causative agent into the circulation numerous pustules appear on the skin (Fig. 64). Soon the pustules become ulcerated. Localization of the affection on the upper or lower lip often results in formation of an inflammatory infiltrate. A rather copious discharge of sanious fluid and pus from the nose is always observed. The temperature rises rapidly to 38.5-39.5°C.

As the disease progresses and bacteraemia develops deep abscesses are formed in the muscles (usually in the gastrocnemius muscles). The fistulae which form at the same time do not close for a long period and continuously discharge greenish pus. Cicatrization at the sites of the fistulae is possible later. The spleen is enlarged, the liver enlarges only in some cases. Bacteraemia and the general septic

condition are responsible for the formation of new pustules and suppurative abscesses. Acute forms of glanders usually end lethally.

Chronic glanders may last several years, being accompanied by affections of the skin, the mucosa of the nose or of the pulmonary tissue. Granulomas, necroses and abscesses form in the lungs and lead to considerable general emaciation. Sometimes the pathologic process in the lungs begins to spread, involving increasingly new portions of pulmonary tissue (creeping pleuropneumonia). Like the



Fig. 64. Acute glanders patient

acute form of the disease, chronic glanders is characterized by formation of new, fresh muscular abscesses and skin pustules. Necroses of considerable portions of the soft tissues of the nose, lips and cheeks are possible.

Glanders does not confer stable immunity.

Diagnosis. Glanders may be diagnosed on the basis of epidemiological data (contact with horses affected with glanders) and the clinical picture of the disease.

The laboratory methods of diagnosis include discovery of glanders bacteria in Gram stained smears from the contents of pustules and microscopy of the discharges from the nose or the sputum stained by the same method. The causative agent may be isolated by inoculation of the contents of pustules and abscesses in broth containing glycerol; the glanders bacteria grown in this medium are transferred to milk and gelatin. Moreover, on about the 8th or 10th day of the disease an allergic test is made by intracutaneous administration of 0.1 ml of mallein (filtrate of a 4-month-old broth culture of glanders bacteria) into the forearm. In positive cases a hyperaemic area (at least 3-4 cm) with infiltration of the skin is formed at the site of mallein administration within 24 hours. This

allergic test is more convenient and simpler than all other methods of laboratory diagnosis.

Differential diagnosis. The disease must be differentiated from tuberculosis, furunculosis and septicopyaemia.

Treatment. All acute glanders patients must be hospitalized (in contagious departments of hospitals).

The attending personnel must observe the rules of personal prophylaxis: hand-washing, disinfection of the patients' sputum (in cases of pulmonary affection), and burning of the bandages soaked in pus from pustules or in other discharges. If the patient has an affection of the lungs, the attending personnel must wear gauze masks covering the nose and mouth.

The treatment is symptomatic. In cases of abscesses it is necessary to resort to surgical intervention. Injections of penicillin are administered to prevent secondary infection.

Prevention. To prevent the disease, it is necessary to exercise daily veterinary control of horses and reveal diseased animals by a conjunctival mallein test. Instillation of mallein in the horse's conjunctival sac evokes in positive cases an acute inflammatory reaction of the conjunctivae with liquid pus oozing out of the corner of the eye. Infected animals are killed because of the futility of their treatment and their contagiousness; their carcasses are buried 3 m deep and covered with calcium chloride, or are burned.

It is necessary carefully to observe all rules of personal hygiene (to wear rubber gloves, special coveralls, aprons, masks, goggles) when tending horses, especially horses suspected of glanders. After wear the working clothes must be soaked in a 0.5 per cent chloramine solution and then boiled; the rubber boots and gloves must be wiped with a similar solution, while the hands must be disinfected with a 0.25 chloramine solution. The litter used by diseased horses must be immediately burned. A 10 per cent calcium chloride solution must be used for current disinfection of stables.

Workers of livestock farms must be periodically instructed on the routes of transmission of glanders and measures of its prevention. Upon appearance of a glanders case among the livestock of a given farm the veterinary control must be increased, the aforementioned measures must be carried out and a quarantine for all the livestock on the farm must be established. Postmortem examinations of humans, as well as animals, who have died of glanders, must be performed with great precautions.

ANTHRAX

The disease is characterized by an epidemic spread.

Under natural conditions anthrax affects livestock, especially cattle.

Brief historical information. The first reliable observations of anthrax in man date from the second half of the 18th century. In 1788 S. S. Andreyevsky (Western Siberia) infected himself from an animal and established the same cause of the disease in man and animals, i.e., the zoonotic origin of anthrax. A description of Andreyevsky's work has been preserved in archives.

The causative agent of anthrax was discovered and isolated in a pure culture by the outstanding German scientist R. Koch in 1876. L. Pasteur developed an anthrax vaccine to immunize animals in 1885 and demonstrated its high immunizing capacity.

A substantial contribution to the elaboration of the problems of immunity to anthrax and to the production of an anthrax vaccine was made by I. I. Mechnikov, G. N. Minkh, A. V. Vladimirov, N. F. Gamaleya and L. S. Tsenkovsky. A corpuscular and chemical vaccines have now been produced for immunizing man.

Aetiology. The causative agent of anthrax is a gram-positive bacterium (*Bacillus anthracis*); it is a rather long rod (5-8 μ long and 1.5-2 μ thick) with perpendicularly "chopped-off" ends. It is aerobic and easily forms spores under unfavourable external conditions; the spores are highly resistant to heat and cold, desiccation and direct sunlight; in the soil they may keep alive for up to 2 years.

In microscopic preparations from the "juice" of anthrax pustules and in pure culture anthrax bacteria stain intensively by the Gram method and easily by methylene blue.

Anthrax bacteria develop well in artificial nutrient media; in broth they produce flakes, and, inoculated in gelatin, they form a downward-pointing herringbone pattern. In a pure culture vegetative forms of these bacteria are destroyed by heating at 80°C for 6-8 minutes; they are killed as rapidly by carbolic acid and mercury bichloride solutions (1 : 1,000). Anthrax spores are highly resistant and are killed only by heating in an autoclave for 2 hours at 120°C.

After gaining entrance into the human organism through the skin, upper respiratory tract or mucous membrane of the gastrointestinal tract the spores of anthrax bacteria develop into the vegetative, bacillary form surrounded by a capsule.

Epidemiology. Livestock is the reservoir of the infection under natural conditions. Man may become infected with anthrax during work (caring for diseased animals, processing leather, furs, wool and bristle of animals infected with anthrax) or merely by wearing, for example, a woollen kerchief containing spores of anthrax bacteria (in this case an anthrax carbuncle may form on the neck). The disease may also be contracted from raw hides or tanned, but not disinfected, leather from anthrax-infected animals.

Infection with anthrax may take place by occupational-agricultural, occupational-industrial and every-day-life routes.

In the USSR anthrax occurs in but single cases and mainly in the cutaneous form; the pulmonary and intestinal forms of the disease are very rare. The sharp decrease in the anthrax incidence in



Fig. 62. Idiopathic hypoparathyroidism (Well-Vandey) - chronic patient

the USSR was brought about by extensive veterinary and sanitary-hygienic measures, especially strict sanitary control of the meat, hides and wool yielded by livestock.

Anthrax-infected animals (mainly cattle and less so hogs) are the reservoir of infection in nature. Humans infected with anthrax are contagious, but their role in the epidemiology of the disease is not so important as that of diseased animals. Under natural conditions man contracts the disease while caring for animals or using their products (meat, wool, hides). The causative agent may gain entrance into the human organism through the skin and through the mucous membranes of the respiratory and digestive tracts.

A certain part in the spread of the infection is played by the soil, especially of water-meadows and marshes, where the spores of anthrax bacteria may be preserved for years. In summer the infection may be spread by horseflies and stable flies. Infection of man by the inhalation method, for example, by inhaling particles of dust while processing wool, may give rise to the pulmonary form of the disease. Consumption of the meat of an infected animal or of contaminated water results in development of the intestinal form of anthrax.

It has been established that a human anthrax patient is not very contagious, but hospitalization and strict isolation of anthrax patients are obligatory regardless of the clinical form of this disease.

Pathogenesis and pathologic anatomy. The pathogenesis of the disease is determined by the general character of the infection (se-rous-haemorrhagic processes in the tissues and organs, febrile reaction and tendency to development of acute septicaemia), the reactivity of the organism (severity of the disease) and the concrete mechanism of infection (possibility of development of a cutaneous, pulmonary or intestinal form of the disease). Postmortem examination of a person who has died of anthrax reveals extreme hyperaemia of the organs. The pulmonary and intestinal forms are accompanied by changes mainly in the corresponding organs (parenchyma of the lungs and bronchi and the walls of the intestines). A picture of haemorrhagic meningitis is not infrequent.

Clinical picture. The incubation period averages 2-3 days, but may last up to 8 days, depending on the route of infection (through the skin, the respiratory or intestinal tracts).

The character of the atrium of infection determines one of the three main clinical forms of the disease—cutaneous, pulmonary and gastrointestinal. Now and then a primary septic form is observed.

The *cutaneous* form in which an anthrax carbuncle (Fig. 65) is formed is the most frequent.

At first a small but very itchy red macule appears on the skin in the region of the atrium of infection; soon the macule develops into a dense nodule—a papule.

Within several hours a vesicle appears on top of the papule.



Fig. 1. A. B. X. carcinoma.

The papule gradually fills with a purulent content and thus changes to a pustule. Then the pustule bursts and leaves necrotic tissues which form a *black scab* (Fig. 66); it looks like coal, hence the designation of the disease—*anthrax* (Latin for coal).

The scab continues to enlarge and sinks. Several small, additional "filial" vesicles form around it and make up a sort of areola



Fig. 66. Anthrax carbuncle on the face and necrosis of the right eyelid

(Fig. 67) surrounding the central black necrotic scab; further along the periphery of the central necrosis massive oedema of the soft tissues develops. The oedema may be very extensive; it develops mainly where there is loose subcutaneous tissue. The extent of the oedema in a certain measure characterizes the severity of the disease. It is characteristic that in the region of the oedema and at the very site of the scab there is absolutely *no sense of pain* on slight pricking with a needle (sterile!) or palpating with a rubber-gloved hand. In the region of the peripheral oedema the skin is tense and lustrous. The black scab (see Fig. 67) is surrounded by a narrow, yellowish, purulent border and, along the periphery, by a slight brown elevation.

In anthrax the rise in temperature varies within very wide limits; the temperature may rise slightly, but in some cases it rises to 40-40.5°C as early as the second day of the disease. The temperature curve is not very regular.

The very first hours of the disease are marked by general indisposition, jadedness, insomnia and headaches. The patients are often in a melancholic, dejected mood.

The foregoing general symptoms are observed not only in the cutaneous form, but also in the other clinical forms of the disease.

As the patient recovers the necrotic scab becomes disengaged and is replaced by young granulation tissue.

Many patients develop regional lymphadenitis following the appearance of a carbuncle. The cutaneous form of anthrax may become complicated by anthrax sepsis with secondary localization of the infection in the endocardium or the meninges (acute haemorrhagic endocarditis, haemorrhagic meningitis).

An anthrax carbuncle usually localizes on exposed parts of the body, especially on the skin of the head and upper extremities.

The pulmonary form of anthrax runs a very severe course. The onset of the pulmonary form is due to inhalation of dust containing vegetative forms or spores of the causative agent.



Fig. 67. Anthrax carbuncle with peripherally located secondary vesicles

The most important symptoms of the pulmonary form of anthrax are respiratory difficulty, chills with a rise in temperature and discharge of rather large amounts of liquid, foamy, pink-coloured and sanguineous sputum.

The patients' sputum abounds in anthrax bacteria.

Examination of patients reveals phenomena of focal pneumonia: dull tympanic sound on percussion and a large number of moist vesicular rales in the affected area of the lung. Pneumonia may be followed by exudative pleurisy. Roentgenological examination of the lungs reveals focal or confluent pneumonia. As in the other forms the disease may develop into acute haemorrhagic sepsis with haemorrhagic meningitis and may end lethally.

The intestinal form of anthrax runs an uncommonly severe course with extreme intoxication of the organism and a frequent sanguineous stool. This form develops acutely. It is characterized by cutting pains in the abdomen, vomiting with bile and blood, considerable meteorism due to intestinal paresis, and elevated temperature. The morbid phenomena rapidly increase so that death may ensue between the 3rd and 5th days of the disease as a result of growing cardiovascular insufficiency and haemorrhagic sepsis.

The direct cause of death in anthrax, especially if the treatment is late or insufficiently vigorous, is acute haemorrhagic (anthrax) sepsis. Modern therapeutic agents have sharply reduced mortality and produce good therapeutic results, especially in the cutaneous form of the disease.

In addition to the aforementioned typical forms, now and then primary septic forms occur (in extremely emaciated and debilitated patients with considerably lowered resistance). An attack of the disease always confers lasting immunity.

Diagnosis. Anthrax may be diagnosed on the basis of an analysis of the clinical data characteristic of the particular form of the disease (cutaneous, pulmonary, intestinal) and epidemiological data (contact with diseased animals, work with contaminated hides and furs, wearing of sheepskin coats and woolen kerchiefs contaminated with spores of anthrax bacteria).

In addition to strict consideration of the clinical and epidemiological data, the diagnosis of anthrax must be confirmed bacteriologically, i.e., by microscopic examination of stained preparations of the contents of carbuncles in the cutaneous form of the disease, and of the sputum in the pulmonary form. It is desirable to make cultures of the sputum, faeces, vomitus, contents of carbuncles and the blood in accordance with the concrete form of the disease in order to isolate anthrax bacteria. The contents of pustules and ulcers are taken with a Pasteur pipette, following which the end of the pipette is soldered. The end of the Pasteur pipette must be placed at the edge of the scab and care must be taken not to injure the tissue by aspirating the juice from the ulcer. After 2 or 3 pipettes

have thus been filled they are put in a wooden box lined with galvanized iron and tightly closed with a lid and locked. The box is sealed together with a covering note containing all necessary data and is sent by special messenger to an appropriate bacteriological laboratory.

The sputum of anthrax patients is collected in a sterile glass vessel with a tight-fitting lid; the faeces are collected in a glass jar or a special container. If the sputum or faeces have to be sent to a laboratory, they must be put in separate well-sterilized containers equipped with a label, closed and sealed. The containers are placed in a box padded with cotton or hay, a covering letter is put in the same box and the latter is sealed.

Thin smears of the patients' sputum or faeces are made on slides; the smears are stained with a water solution of methylene blue. Anthrax bacteria are Gram-positive. To reveal capsular forms of the bacteria, Roebiger's stain is used; to reveal spores, the preparation is stained by Pashkov's method.

Microscopy of stained preparations reveals large rods with ends cut off at a right angle, surrounded by capsules and arranged in a row of short chains.

The immobility of true anthrax bacteria (essential difference from the banal anthracoid or pseudo-anthrax bacteria which are widespread in nature - in the soil, water and dust) is ascertained by their examination in a hanging drop.

For bacteriological examination the tested material is inoculated in Petri dishes containing meat-peptone agar ($pH=7.2-7.6$). After 20-24 hours in a thermostat at $37^{\circ}C$ the surface of the agar shows rough, lustreless colonies with fluffy edges.

Animal material, for example leather, suspected of contamination with anthrax bacteria is examined by means of the Ascoli precipitin test.

In establishing a *differential diagnosis* it should be remembered that, unlike anthrax carbuncles, ordinary furuncles and carbuncles caused by staphylococci are characterized by a discharge of pus, extreme hyperaemia and pain in the affected tissues.

If the pulmonary form of anthrax is suspected, it should be differentiated from the pulmonary form of plague and from croupous pneumonia. The pulmonary form of plague is characterized by an excited delirious state, frequent coughing with a plentiful discharge of bloody sputum, extreme tachycardia, vomitus containing blood, and presence of plague bacteria in stained preparations of sputum; corresponding epidemiological data must also be taken into account.

Croupous pneumonia is characterized by an acute onset, high temperature, pains in one half of the chest (usually in a side), a lag of the affected side in respiration, shortened percussion sound with a bronchial shade and crepitant rales. The sputum is scant, thick, rusty, less frequently sanguineous.

The intestinal form of anthrax must be differentiated from severe food infections and toxic dysentery.

Treatment. The principle agent in the treatment of anthrax patients is *penicillin* which must be administered intramuscularly in a dose of 400,000 U 3 times per day until a complete clinical effect has been produced (but at least for 7-8 days). In severe forms of the disease, especially in cases of pulmonary and intestinal anthrax, the dose must be increased to 1,600,000 U per day and administered intramuscularly with additional administration of streptomycin (250,000 U twice a day).

Treatment with biomycin, tetracycline or terramycin is less effective, but, if one of these agents is chosen, it should be administered per os in a dose of 0.3 g 4 times (i.e., 1,200,000 U) per day.

Treatment of anthrax patients simultaneously with a number of agents is particularly desirable; penicillin supplemented in severe cases with streptomycin is administered as the principal therapeutic agent to which anti-anthrax serum and novarsenol (neoarsphenamine) must be added.

The anti-anthrax (antibacterial) serum is administered intramuscularly in doses depending on the severity of the case and the form of the disease (50-200 ml per day). The first time the serum is administered by the method described on page 75 or by Besredka's method. Administration of the serum once a day must be repeated also during the following 3-4 days of the treatment. During the period of treatment with the serum and penicillin it is necessary to give the patient two or three intravenous injections (at 48-hour intervals) of 0.45 g of novarsenol; before administration the dose of the drug must be dissolved in 10 ml of twice-distilled sterile water; the solution must be administered slowly (over a period of 2 minutes).

In cases of marked intoxication 400-500 ml of physiologic solution is administered into the subcutaneous tissue of each thigh daily for 4-6 days; in addition, the patient must be given intravenous infusions of a 40 per cent glucose solution (50-75 ml) and subcutaneous infusions of a 5 per cent glucose solution in a dose of 400 ml, preferably by the drip method. The patient must also be given large doses of vitamin C (300-500 mg per day).

The treatment of the cutaneous form of anthrax produces better results than does the treatment of the pulmonary and, especially, the intestinal forms. The presence of cardiovascular disturbances necessitates injections of ephedrine, cordiamine, caffeine and camphor (in the usual therapeutic doses).

Anthrax patients must be isolated in separate wards or compartments. The attending personnel must strictly observe all rules of personal precaution; they must wear rubber gloves and, if the patient has the pulmonary form of anthrax, gauze masks, covering the mouth and nose, and goggles. Thorough current disinfection

must be carried out at the patient's bedside. In cases of the pulmonary or intestinal forms of the disease it is necessary to disinfect the sputum with a 3 per cent lysol solution and the faeces with a 10 per cent calcium chloride solution respectively. All of the dressing material used must be burned.

After the discharge of a convalescent his ward or compartment is given the final disinfection.

Prevention. The main preventive measures are veterinary control of livestock, check-up on the Ascoli test, disinfection, if necessary, of all the raw material of animal origin (leather, wool, bristle) to be processed, isolation of the patients and their rational treatment, and specific inoculations of animals with a living vaccine epicutaneously or with a chemical vaccine (protective antigen).

People who are in immediate danger of infection—zootechnicians, veterinarians, cattle-breeders, workers of the leather and fur industries and of bristle processing enterprises—must be inoculated with the anthrax vaccine epicutaneously.

To reveal the contamination of hides and of articles made of hides, fur and bristle (sheepskin coats, fur collars and hats, shaving brushes, etc.) the Ascoli precipitin test is used. Harness, saddles and other leather articles are disinfected by pickling, while fur coats, sheepskin coats, fur hats, wool and woolen articles are disinfected in formalin vapour chambers.

Pickling consists in soaking leather for a long time (24 hours and longer) in a mixture of a 1 per cent pure hydrochloric acid solution and a 10 per cent sodium chloride solution at a temperature of 20-25 C.

The meat of anthrax-infected animals must under no circumstances be used as food. People who had any skin injuries while dressing anthrax-infected carcasses or consumed infected meat must be given a prophylactic injection of 100 ml of antianthrax serum subcutaneously and 3 subcutaneous injections of 300,000 U of penicillin at 4-hour intervals.

To prevent the pulmonary form of anthrax, the people working with wool must wear respirators; workers of tanneries must wear rubber gloves.

People recovering from the cutaneous form of anthrax may be discharged from the hospital after disengagement of the scab and complete epithelization of the ulcer.

Clinical recovery serves as a guide for discharging people convalescing from the pulmonary and intestinal forms of anthrax; two negative tests (at a 5-day interval) for anthrax bacteria of the pulmonary anthrax patient's sputum and of the intestinal anthrax patient's faeces serve as adequate grounds for discharge.

Postmortem examinations of the corpses of people who have died of anthrax must be performed with special precautions.

The carcasses of animals who have died of anthrax must be buried

at least 2 m deep in nonfloodable places far from populated areas; the bottom of the grave and the carcass of the animal must be covered with a heavy layer of dry chloride of lime.

TULARAEMIA

Tularaemia is a zoonotic disease, i.e., it is transmitted to man by infected animals. Wild rodents are the main reservoir of the infection in nature.

The disease is characterized by a cyclic course, febrile period, various localization of the pathologic process and inevitable affection of the regional lymph nodes.

Brief historical information. In 1877 Russian physicians observed a transmissive outbreak of tularaemia in Astrakhan, but the disease was described in detail by E. Francis in 1921. The causative agent of the disease was isolated in the state of California (USA) in 1912 by G. McCoy and W. Chapin, while they were studying epidemics among rodents and in humans in Tulare County (California); the disease (tularaemia) was named after the county. In the USSR regular studies of tularaemia began in 1926-1930. Soviet investigators have obtained many important scientific data on the aetiology, epidemiology, diagnosis, clinical aspects and therapy of this disease. N. A. Gaisky produced a living tularaemia vaccine (1945), A. A. Volferits, A. N. Berinskaya and G. P. Rudnev studied the clinical aspects and routes of transmission of the infection, and N. G. Olsufyev investigated the microbiology and epidemiology of the disease.

Aetiology. Tularaemia is caused by a short sporeless bacillus (*Pasteurella tularensis*) which is very well preserved in the external environment. The bacillus may long remain viable in carcasses or hides of infected animals and in foodstuffs. The most favourable artificial nutrient medium for cultivating tularaemia bacteria is one containing the yolk of a chicken egg.

Sources and routes of transmission of the infection. Tularaemic infection is retained in the organism of infected rodents — field mice, jerboas, rabbits, musk-rats, gophers and water rats (Fig. 68) from which it may be transmitted to susceptible humans. The routes of transmission of tularaemia vary. The following principal routes are known: (a) contact (for example, by skinning killed rodents), (b) water, (c) alimentary, (d) inhalation (inhaling dust contaminated by the urine of rodents), and (e) transmissive (through infected insects and arthropods).

An important part in the epidemiology of tularaemia is played by the fact that with the urine of infected rodents tularaemia bacteria may gain entrance to open water reservoirs, foodstuffs and grain stacks in the field. During threshing of grain contaminated with tularaemia bacteria man may contract the disease by inhaling dust containing the bacteria or may become infected with the oculobubonic form of tularaemia as the result of the causative agent lodging itself on the conjunctivae of the eyes.

The anginous-bubonic and abdominal forms of tularaemia are contracted by consumption of water or foodstuffs contaminated

by rodents. The infection is much less frequently transmitted from infected rodents through bites of blood-sucking insects and arthropods (horse-flies, stable-flies and certain species of ticks). A tularaemia patient is practically noncontagious to the people around him.

Tularaemia is characterized by certain seasonal incidence: the ulcerative-bubonic and bubonic forms most commonly occur in spring in connection with hunting water rats. The incidence of human anginous-bubonic and bronchopulmonary forms of tularaemia may rise at the end of summer and in autumn when the incidence of tularaemia increases among wild rodents.

According to A. A. Maximov (1960), the following types of natural tularaemia foci must be distinguished: (a) marsh-lake-river, (b) steppe (mice), (c) meadow and field, and (d) tundra.

To characterize the types of tularaemia incidence, I. N. Maisky and N. G. Olsufyev (1960) suggest the following classification of these types: (1) communicable, (2) trade, (3) hunting and alimentary, (4) water, (5) agricultural, (6) household, (7) food, (8) industrial and (9) trench.

Pathogenesis. The existence of various routes of transmission of the infection to man is responsible for the variety of the clinical manifestations of tularaemia. Small tissue necroses with formation of the *primary affect* arise at the atrium of infection. Transitory bacteraemia due to generalization of the infection develops at the end of the incubation period and in the very beginning of the febrile period of the disease.

Regional lymphadenitis, a must element of the pathogenesis of tularaemia, forms soon afterwards. The subsequent course of the disease depends on the character of the general pathologic symp-



Fig. 68. Water rat

toms (febrile reaction, intoxication, disturbances in cardiovascular functions) determined by the circulation of the causative agent in the blood and the partial disintegration of the causative agent; to a certain measure it is also determined by the development of anatomic processes in the region of the atrium of infection and the regional lymph nodes.

Incubation period. The incubation period averages 6-8 days, but may vary from 3 to 21 days.

Classification. According to official classification, there are mild, moderately severe and severe cases of tularaemia, and acute, protracted (lasting more than 1.5 months) and relapsing forms of the disease.

The predominant localization of the affections is given in the classification as follows: (1) tularaemia with affections of the skin, mucous membranes and lymph nodes: (a) ulcerative-bubonic, (b) bubonic, (c) oculobubonic, (d) anginous-bubonic, and (e) tularaemia with affection of the mucous membranes of the nose and mouth; (2) tularaemia with predominant affections of internal organs: (a) the respiratory system (bronchopulmonary form), (b) gastrointestinal tract (abdominal form); (3) generalized form of tularaemia.

Clinical course. Whatever the clinical form of the disease, it sets in acutely with chills and a rise in temperature. Patients complain of headache, diminished appetite, sleep disturbances and general jadedness. Hyperaemia of the face and excessive sweating are often observed. A roseolous or papular eruption may break out mainly on the lower extremities.

The temperature curve is most commonly (in 60-80 per cent of the cases) of a remittent character, often with considerable variations over a period of 2-3 days.

The febrile period averages a total of 15-18 days, but sometimes may be prolonged to 3-4 weeks and even longer.

The temperature curve and haemogram reflect the suppurative processes in the regional lymph nodes, changes in the region of the atrium of infection, and development of general granulomatosis.

In typical cases the blood picture is characterized by leucopenia or normocytosis with a moderate shift to the left and relative lymphocytosis with a somewhat accelerated ESR.

In the *ulcerative-bubonic form* a sharply circumscribed red maculo appears on the skin at the atrium of infection first; the macule transforms into a papule with subsequent development of a vesicle of epidermal necrosis and a small ulcer in its centre (Fig. 69); simultaneously the *regional* lymph node enlarges (bubo), for example, in the axilla, on the neck (Fig. 70) or in the inguinal region, in accordance with the atrium of infection. It is characteristic that the ulcers form on exposed parts of the body (hands and forearms, forehead, head and neck). The ulcers are superficial and reach 10-12 mm in diameter.



FIG. 69. Tularemia: primary ulcer on right forefinger (ulcerative-bubonic form)



FIG. 70. Patient with bubonic form of tularemia

The enlarged lymph nodes are somewhat compact and slightly painful, but do not adhere to each other; separate nodes form packets. Subsequently the buboes may dissolve or become considerably indurated; during late periods of the disease they may soften and form fistulae long discharging pus.

Bubonic tularaemia is another frequent clinical form of the disease; no visible changes are observed near the atrium of infection on the skin or mucous membranes since the causative agent rapidly penetrates into regional lymph nodes where it produces a number of characteristic pathologic changes (lymphadenitis). The bubonic form is the most typical among water rat hunters.

The most commonly affected lymph nodes are the elbow and axillary nodes, and sometimes the inguinal nodes; the nodes often enlarge to the size of a hazelnut or even a walnut. Several enlarged lymph nodes located next to each other form a package; the nodes are scarcely painful, do not adhere to each other or to the surrounding cellular tissue, and are freely movable. The dissolution of buboes begins after normalization of the temperature and lasts 12-25 days and even longer. In some cases the buboes become indurated and sclerosed and their dissolution may be retarded for a long time. In cases of late or inadequate treatment with antibiotics a purulent dissolution of buboes is possible; in such cases the skin over buboes grows red, and a fluctuation is clearly observed. If no incision is made, a long-unhealing fistula is formed and thick creamy pus is discharged.

Drinking water contaminated with tularaemia bacteria (for example, from closed water reservoirs) may cause the *anginous-bubonic form* of tularaemia which is characterized by formation of yellowish-grey islet and confluent necrotic films on the tonsils with subsequent ulceration of the tonsils, enlargement of the submaxillary and anterior and posterior cervical lymph nodes (Fig. 70). The affection of the tonsils is usually one-sided. Now and then the pharynx is affected.

When the harvest is late and stacks of cereals remain in the field they may become contaminated with the urine of rodents (ordinarily, field mice) infected with tularaemia. Inhalation of particles of dust containing tularaemia bacteria during threshing may lead to infection with the *pulmonary* (or bronchopulmonary) form of tularaemia. The aforementioned forms of the disease exhibit a picture of focal pneumonia whose tularaemic aetiology may be established by roentgenological examination of the lungs with a simultaneous tularin (tularaemia allergen) allergic skin test. To reveal the enlargement of the mediastinal lymph nodes, especially bronchopulmonary nodes (tularaemic bronchadenitis), by roentgenoscopy and roentgenography, it is necessary to examine the patient in oblique positions I and II. The *oculobubonic* and *intestinal* (abdominal) forms of tularaemia are infrequent. The oculobubonic

form (Fig. 71) is accompanied not only by such general phenomena, as elevated temperature, headache and indisposition, but also by swelling of the lids, follicular growths on the conjunctiva of the affected eye and development of regional lymphadenitis in the region of the corresponding parotid gland.

The intestinal form of tularaemia is very difficult to diagnose. In addition to certain general phenomena, similar to those just described, intestinal tularaemia patients usually react positively to the tularin allergic skin test and agglutination test of their blood serum to a killed tularaemia culture in 1 : 160 and greater dilutions.



Fig. 71. Patient with oculo-bubonic form of tularaemia

The febrile period of tularaemia usually does not exceed 16-18 days; in streptomycin-treated cases it is shorter, but the resorption of the buboes is usually retarded. The disease is followed by a number of months of diminished working capacity, general indisposition, loss of strength and of appetite.

An attack of the disease confers lasting immunity, although early relapses are possible. Sometimes tularaemia runs a protracted course and lasts 2-3 months.

Diagnosis. Tularaemia is diagnosed on the basis of the clinical picture of the disease and epidemiological data, and in the pulmonary form also on roentgen data. The diagnosis is confirmed by an allergic skin test and an agglutination test with a killed tularaemia culture; the skin test is performed as follows.

A 0.1 ml dose of *tularin* is administered into the forearm intracutaneously with a syringe having a thin needle. Erythema of the skin

measuring 3×4 cm (and even more), swelling and infiltration may be observed in a tularaemia patient at the site of the injection 24 hours later. Sometimes necrosis develops in the centre of the hyperaemic area; lymphangitis and regional lymphadenitis are possible. By this test the diagnosis of tularaemia may be confirmed quite early—between the 5th and 7th days of the disease.

The allergic skin test with tularin is strictly specific. An epicutaneous test with tularin containing 2,000,000,000 microbial bodies per 1 ml of the preparation has been additionally suggested for allergic diagnosis. The results are appraised in 48 hours.

From the 8th or 9th day of the disease an agglutination test with a killed culture of tularaemia bacteria can be used in diagnosing tularaemia; the test is made in test-tubes. The minimum diagnostic titre is a 1 : 160 dilution of the serum with subsequent increase in the titre during tests repeated within 3-4 days necessarily with complete or almost complete agglutination of the bacteria (++++ or +++ reaction).

In the absence of a local laboratory, where the agglutination test may be performed, two or three drops of blood are taken from the patient's finger, are dried on a strip of cellophane and then sent in an envelope to the closest laboratory.

Differential diagnosis. In cases where there are corresponding epidemiological data the disease must be differentiated from bubonic and pulmonary plague (see the chapters treating of these diseases and Table 4); it is additionally necessary to differentiate this disease from tuberculosis of lymph nodes and from lymphadenoses.

The anginous-bubonic form should be differentiated from catarrhal, follicular and other forms of angina, including Vincent's angina, necroses of the fauces in agranulocytic angina, and mononucleosis. If the bronchopulmonary form of tularaemia is suspected, it should be differentiated from pneumoniae of various aetiology with the aid of a roentgenological examination and an allergic skin test with tularin.

Treatment. Even in the absence of treatment tularaemia runs a rather favourable course, and mortality does not exceed 1 per cent. The use of antibiotics has brought mortality down almost to zero. The best results are produced by treatment with streptomycin (0.5 g twice a day intramuscularly for 6-8 days). Biomycin is used with a good therapeutic effect (300,000 U 4 times per day for 6-8 days). In severe cases it may be combined with streptomycin.

The disease may also be treated with tetracycline (0.3 g 4 times a day for 6-8 days).

It is advisable to treat all forms of tularaemia with streptomycin by individualizing the doses and duration of the therapeutic course. If the disease runs a protracted course, it is desirable, in addition to antibiotics, to administer subcutaneously the tularaemia vaccine in single doses ranging from 50,000 to 25,000,000 microbial bo-

Table 4

Table of Differential Diagnosis of Bubonic Forms of Tularaemia and Plague

Symptom	Bubonic form of tularaemia	Bubonic form of plague
Onset of disease	Acute; chills or chilliness, rapid rise in temperature to 39-39.5°C in the beginning of the second day; subsequently, remitting-type temperature curve until the 15th-20th day During the first days of the disease—general jadedness, headache, insomnia, poor appetite	Acute; chills, rise in temperature to 40-41°C within a few hours, grave general condition, extreme weakness, in some cases—vomiting. Continuous headache, dizziness, insomnia. During the days immediately following the onset the temperature remains at a high level
Consciousness	Usually retained (except in individual severe cases)	In some cases the consciousness is clouded, the patient is excited, the face shows suffering and horror. Delirium is possible
Patient's general condition	Not so serious as in plague	Much more serious than in tularaemia. Extreme toxicosis
Cardiovascular system	Pulse rate corresponds to the temperature level Slight hypotension, heart sounds moderately dull	Tachycardia (pulse rate 140-160 per minute). The pulse is soft; the blood pressure drops. The heart borders are sometimes extended The heart sounds are usually very dull; systolic murmur and embryocardia are

Tongue	During the first days moist, moderately coated with a white film	Characteristically dry, heavily coated with a white film (chalk tongue)
Regional lymphadenitis (bubo) and its predominant localization	Visible enlargement of regional lymph nodes is revealed on the second or third day of the disease. The enlargement is preceded by painfulness. Several nodes located near each other form a "package"; they are scarcely painful, do not adhere to each other or to the surrounding cellular tissue, and are mobile	The bubo is formed by enlargement of several adjoining regional lymph nodes with development of marked periadenitis. The bubo is painful, of densely-elastic consistency, and the skin above it is inflamed or necrotizing. Most commonly it undergoes purulent dissolution, but may also be completely resorbed The size of the bubo greatly varies
	Periadenitis is not pronounced. The enlarged nodes reach the size of a hazelnut or even a walnut. Subsequently the buboes are most commonly resorbed, but may suppurate and sclerose Elbow and axillary buboes are the most frequent	Tendency to development of hemorrhagic septicaemia with possible formation of secondary buboes and onset of metastatic plague pneumonia. Inguinal buboes are the most frequent

dies. A total of 8 injections at 3-day intervals should be made. Suppuration of a bubo requires an incision, an aseptic dressing and injections of penicillin and streptomycin.

Prevention. Extensive health education of the inhabitants of the areas where tularaemia occurs plays an important part in the prevention of this disease. To reveal mass incidence of tularaemia among rodents requires epizootic observation.

An important role is played by mass extermination of the rodents and prevention of their access to water reservoirs, wells and food-stuffs.

Drinking raw water from open water reservoirs (in fields and woods) is strictly prohibited. Every precaution must be taken in skinning water rats.

In controlling rodents—the reservoir and carriers of the infection—no straw or chaff must be left in the fields. To prevent field mice from nestling in haystacks, ditches 40 cm wide and 40 cm deep must be dug around the stacks.

In areas with tularaemia incidence among rodents the bottom layer (30-35 cm) of the stacks must not be threshed, but must be burned. Threshers working on contaminated stacks must be supplied with gloves, protective masks and goggles; these precautions are particularly necessary in late harvesting and threshing. Zinc phosphide should be used to exterminate rats.

For specific prevention of tularaemia N. A. Gaisky, a Soviet scientist, developed a method of producing a living tularaemia vaccine from a special strain of tularaemia bacteria in 1945. The vaccine was further studied in detail by B. A. Elbert. The vaccination is administered to people who may contract the disease in virtue of their occupation. The vaccine is dissolved in sterile physiologic solution directly before administration. A drop of the dissolved vaccine is applied to the skin of the upper arm and a double incision is made through this drop with a vaccination lancet. The results of the vaccination are checked in 10-12 days; in positive cases the site of the incisions exhibit erythema, swelling and minute pustules.

Inoculation with the living vaccine confers immunity within 2-3 weeks, the immunity lasting 3-5 years.

PLAGUE (PESTIS)

Plague is a particularly dangerous general infectious disease caused by a special species of bacteria (*Pasteurella pestis*) which belongs to the group of causative agents of haemorrhagic septicemia; the disease is accompanied by considerable general intoxication, a septicohaemorrhagic process, reaction of the lymph nodes (buboes) and affection of the skin and lungs (in accordance with the atrium of infection).

Brief historical information. The plague has occurred since antiquity. Devastating epidemics of this severe disease repeatedly occurred in Europe during

the Middle Ages and in modern times. The principal measures of controlling plague were elaborated as early as the second half of the 18th century by D. S. Samoilovich and A. A. Shafonsky.

The clinical picture of plague was described in detail by physicians, particularly by the Russian army physician A. Charukovsky, in the first half of the 19th century.

The causative agent of the disease was discovered in 1894 by Yersin and Kitasato.

An important contribution to the elaboration of problems of epidemiology, epizootology and natural foci of plague was made in the beginning of the 20th century by D. K. Zabolotny and V. I. Isayev and subsequently by a number of Soviet authors.

The production of the highly effective antibiotic streptomycin (1944) has made it possible to treat this severe disease.

Aetiology. The causative agent of the disease is the plague bacterium (*Pasteurella pestis*); it is a slightly ovoid bacillus 0.5-1.5 μ long and 0.5-0.6 μ thick. It is nonmotile, sporeless and gram-negative. With methylene blue or fuchsin the plague bacteria stain the most intensely at their poles.

The plague bacteria develop well in artificial nutrient media. The causative agent long retains its viability in the corpses of people and carcasses of animals, who have died of the plague, in the sputum of pulmonary plague patients and in the pus of buboes. It resists low temperatures for a long time and very well tolerates freezing.

Boiling rapidly kills the plague bacteria; disinfectants (a 3 per cent lysol solution and a 1 : 10 carbolic acid solution) kill them in 5-6 minutes.

Epidemiology. Wild rodents (tarbagans, jerboas, marmots, gophers, gerbils and field mice) are the reservoir of the infection; in seaports rats may also serve as the reservoir of the infection. Plague is an infectious disease with natural foci, and its spread among rodents determines the possibility of human infection.

Man may contract the disease from rodents by direct contact with them or (more commonly) through fleas (mainly *Xenopsilla cheopis*) which transmits the infection from diseased rodents to man.

The infection may be transmitted from bubonic plague patients to healthy people through the pussy discharges from buboes; in the pulmonary form of plague the sputum is extraordinarily contagious and the disease is transmitted by the air-borne (or droplet) method.

Each case of plague must be immediately reported to the health services. The appearance of even a single case of plague calls for a quarantine.

Pathogenesis and pathologic anatomy. The causative agent may gain entrance into the human organism through the skin, mainly through bites by infected fleas (bubonic plague), through the air (pulmonary plague) and through the gastrointestinal tract (intestinal plague).

Bubonic plague is characterized by a haemorrhagic inflammation in the lymph nodes, regional with respect to the atrium of infection; as the disease progresses the buboes develop necroses, suppurate and form fistulae. Formation of secondary buboes unconnected with the atrium of infection (septicaemia) is possible.

Pulmonary plague is marked by development of foci of haemorrhagic pneumonia and numerous necrotic foci surrounded by areas of hyperaemic pulmonary tissue.

Buboes in the mesenteric lymph nodes are typical of the intestinal form of plague.



Fig. 72. "Chalk" tongue in plague patient (from Mohr)

In any form of plague the disease develops into haemorrhagic sepsis with affection of various organs; death may be due to acute circulatory insufficiency.

Clinical picture. Owing to a number of special features which characterize the different forms of this disease each of them must be considered separately.

Bubonic form. The incubation period is 2-3 days; sometimes it is prolonged to 6 days. The disease sets in acutely with chills, a rapid and considerable rise in temperature, extreme general weakness, headache and vomiting. The consciousness is often clouded; some patients are delirious. The pulse is small and feeble, the blood pressure drops sharply, the heart sounds are very dull, and embryocardia is possible. The tongue coated with a heavy white film—chalk tongue (Fig. 72)—is a characteristic symptom.

No changes in the skin or underlying tissues are observed at the atrium of infection (the site of the bite by an infected flea).

The regional (with respect to the atrium of infection), most commonly inguinal lymph nodes, enlarge and become *plague buboes*

(Fig. 73). In the course of 4-5 days, at a constantly high temperature (39.5-40.5°C), the buboes may necrotize, soften and form fistulae through which pus is discharged; the fistulae close slowly. In some patients, especially in cases of early and vigorous treatment, the buboes are resorbed without suppurating. Even without any antibiotic treatment the bubonic form of the disease usually ends in recovery, although in some cases it ends lethally or develops into acute haemorrhagic sepsis; the latter, as a rule, ends in death.



Fig. 73. Bubonic form of plague (from Mohr)

Sometimes plague buboes long fail to be resorbed, become very compact and, as it were, sclerotic.

Owing to the bacteraemic process in the bubonic form of plague secondary buboes may form in addition to the regional bubo; this form of the disease may also be accompanied by metastatic pneumonia and multiple pustular eruptions all over the skin.

Primary pulmonary plague. This is one of the most severe forms of the disease; it is an air-borne infection transmitted on close contact of a healthy person with a patient affected with primary or secondary pulmonary plague. The patient is discomforted by a cough, pain in the chest (pleuropneumonia), high temperature (up to 41°C) and discharge of sputum.

The percussion and auscultation data revealed by examination of the patient are suggestive of focal pneumonia or pleuropneumonia; however, these data are rather scant and do not correspond to the patient's general grave condition.

In the beginning the sputum is clear, glasslike, foamy and viscous (because it contains fibrin); it is less frequently of a muco-

purulent character. From the second day of the disease the sputum becomes thin and pink or red, depending on the amount of blood it contains. The sputum is often discharged in enormous amounts and contains a mass of plague bacteria. High temperature, extreme intoxication, cardiovascular dysfunction, a chalk tongue (see Fig. 72), extreme excitement, delirium and aggression are all characteristic of this form of plague. The disease lasts from 1-2 to 3-5 days and usually ends lethally. Pulmonary plague rarely occurs without a discharge of sputum.

The intestinal form of plague is rare and is accompanied by extreme intoxication and frequent mucosanguineous stool. It usually ends lethally, but, if the patient survives, it confers rather lasting immunity.

Cutaneous form. This is the rarest clinical form of plague. Very painful pustules, ulcers and carbuncles develop at the atrium of infection. Vast necrotic lesions of the skin are possible. If this form of the disease becomes complicated by septicaemia, secondary pustules and ulcers, unconnected with the primary localization of the process, appear.

Cutaneo-bubonic form. This form is characterized by a combination of the pathologic process on the skin and development of regional lymphadenitis; it occurs much more frequently than the preceding form. As a rule, no lymphangitis develops.

Diagnosis. To diagnose any of the clinical forms of plague, it is exceptionally important to consider the epidemiological data, existence of epizootics in the area of the patient's sojourn and his possible contacts with rodents or plague patients. It is also necessary to take into account the acute, abrupt onset of the disease, the extreme intoxication and high temperature.

In bubonic plague, unlike most cases of ulcerative-bubonic and bubonic forms of tularaemia, there are no changes on the skin at the atrium of infection, the softening and purulent dissolution of buboes occur earlier, and the patient's general condition is grave (Table 4).

If the pulmonary form of plague is suspected, it is necessary to differentiate the disease from the pulmonary form of anthrax and from croupous pneumonia.

All cases require bacteriological confirmation of the diagnosis (cultures of the contents of buboes and blood in the bubonic form, and of the sputum in the pulmonary form of the disease).

A special metal box with a closely-fitting lid is used for the transportation of the contagious material taken from the patient. The closed sterile glass vessel containing the material must be wrapped in gauze soaked in a 10 per cent lysol solution. Laboratory workers must be equipped with a complete antiplague outfit.

If the patient has pustules on the skin, their content is aspirated as follows: the needle of a syringe is introduced at the edge of the

pustule and is moved towards its centre, the syringe drawing in the fluid from the pustule. From the aspirated material smears are prepared for bacteriological examination.

Before taking the juice from a bubo the skin over it is wiped with a cotton tampon moistened in alcohol. Then, observing the rules of asepsis, the needle of a 1-g "Record" syringe is introduced deep into the bubo and with a slow rotatory movement of the sucker a little of the juice is aspirated. If this operation fails to aspirate enough juice, it is necessary to inject into the bubo with the same syringe 0.2-0.3 ml of sterile physiologic solution and with a reverse movement of the sucker aspirate from the bubo an opalescent fluid.

With the same needle and syringe one drop of juice from the bubo is placed on each of 2-3 slides, and smears are made: the smears are dried in the air and are stained by the Gram method. Microscopy reveals ovoid bacteria often more intensively stained at their poles.

Bubo juice is inoculated in agar plates containing (0.3 per cent of their weight) defibrinated rabbit or horse blood; rough colonies with a darker brown or greyish-white somewhat elevated centre appear on the agar plates within 24-30 hours of growth. The smears prepared from these colonies and stained by the Gram method are examined for bacteria under the microscope (the bacteria are discoloured).

At the same time, for purposes of identification with the causative agent of plague, the agglutinability of the isolated bacteria with a specific serum and their lysis by a specific bacteriophage are tested.

The little juice remaining in the syringe after the puncture of the bubo is diluted in the same syringe with 4 ml of sterile physiologic solution and then administered to two guinea pigs intraperitoneally or subcutaneously. The animals die exhibiting a typical pathomorphological picture of haemorrhagic sepsis; plague bacteria may be isolated from their organs.

To confirm the diagnosis of the septic form of plague, it is necessary to take from the ulnar vein 5 ml of blood and inoculate 1 ml of it in the afore-mentioned agar plates and 3 ml in 125 ml of meat-peptone broth (containing 2 ml of haemolysed rabbit, ram or horse blood); moreover, 1 ml of the blood must be administered intraperitoneally to 2 guinea pigs which die exhibiting phenomena of haemorrhagic septicaemia. The growth of plague bacteria in the broth is characteristic: they appear as flakes forming a loose precipitate on the floor of the vial and suspended in a clear liquid.

In the pulmonary form of plague the sputum collected in a sterile cup is immediately examined, for which purpose smears are made on slides, stained by the Gram method and microscopied, an inoculation is made in the afore-mentioned agar plates, part of the sputum is emulsified by a sterile physiologic solution in a 1 : 2

volume ratio and 2 ml of this emulsion is administered intraperitoneally to guinea pigs (the pigs soon die exhibiting phenomena of haemorrhagic septicaemia). In all cases the material for bacteriological examination must be taken from the patient before the beginning of antibiotic treatment.

Prognosis. With the modern methods of treatment, especially in cases of bubonic plague, if the treatment is early and vigorous, the prognosis is favourable. In cases of primary pulmonary plague the prognosis is much more serious.

Treatment. All patients are subject to strictest (and if possible individual) isolation in specially adapted hospitals. Thorough current disinfection with an 8 per cent lysol solution is carried out at the patient's bedside. After recovery of plague patients and their discharge from the hospital, as well as in cases of death, all personal effects which were used by the patients are disinfected and the things which are of little value must be burned. The corpses of people who have died of plague must be cremated; if they are buried, the graves must be at least 2 m deep, the bottoms of the graves must be covered with a layer of chloride of lime; the coffins must also be covered with chloride of lime before they are covered with earth. In cases of pulmonary plague or metastatic pneumonia the sputum must be disinfected with an 8 per cent lysol solution; the dishes used by patients must be immersed for 2 hours in a 3 per cent chloramine solution and then boiled.

The personnel attending plague patients must wear protective coveralls, rubber boots and gloves, special masks and goggles.

The treatment of plague patients with antibiotics and drugs must begin as early as possible. Good results are produced by treatment with massive doses of streptomycin (1,000,000 U 3 times per day intramuscularly for 7-9 days); in cases of pulmonary and intestinal plague the daily dose is increased (3.5-4 g of streptomycin per day during the first 3 days of treatment and then 2.5-3 g per day). Some 20-26 g of the antibiotic is administered per course of treatment. The injections of streptomycin may be combined with sulpha drugs administered per os. In severe cases an antibacterial serum is administered (100-200 ml per day) in addition to streptomycin. In order to support the cardiovascular functions it is advisable to give the patients injections of ephedrine combined with camphor. Plentiful subcutaneous and drip intravenous infusions of physiologic solution and 5 per cent glucose solution are helpful.

An attack of the disease confers lasting immunity.

Plague convalescents may not be discharged from hospital before one month has elapsed since the disappearance of the clinical symptoms. In cases of bubonic and cutaneo-bubonic forms of the disease it is additionally necessary to obtain negative results from bacteriological examination of two specimens produced by punctures of the buboes at 2-day intervals after the 15th day from the time of

disappearance of the plague symptoms. In cases of pulmonary plague and metastatic pneumonia patients are discharged only after examinations of the sputum for plague bacteria have repeatedly yielded negative results. All persons who have had any contact with a patient are subject to individual isolation for 9 days and, if these persons have been administered antibacterial serum, the isolation is prolonged to 12 days.

Prevention. Since the plague incidence among humans is closely connected with the epizootological situation it is necessary that the antiplague stations located in endemic foci should continuously watch out for a possible spread of plague among rodents.

In seaports quarantine measures are carried out whenever necessary to prevent plague from being brought in by ship rats.

Rats are exterminated with zinc phosphide and the use of traps. Wild rodents are exterminated with chloropicrin, especially if there is any danger of plague being spread from endemic foci; good results are also produced by dusting the burrows of wild rodents with zinc phosphide and zoocoumarin (3-[2-phenyl-2-acetyethyl] 4-oxy coumarin).

Upon discovery of even a single case of plague it is necessary to establish a quarantine over a sufficiently large territory surrounding the place where the case has been discovered; a special way of supplying the population of the given community with the necessities of life must be established, and people should be allowed to enter and leave only by special permit.

To exterminate fleas, dwellings and production buildings should be dusted with a 10 per cent DDT powder or hexachloreyclohexane (8 g of powder per 1 square metre of floor space). Gas disinsection with chloropicrin (15-20 ml per 1 cu m of space for 24 hours provided the premises are made airtight) is even more effective.

The rules of hospitalization have already been dealt with. All the attending personnel must be thoroughly instructed and provided with special protective coveralls, goggles, and rubber boots and gloves. Postmortem examinations of people who have died of plague are made with great precautions and according to special instructions.

The following measures are necessary to liquidate a circumscribed plague focus:

(1) strict isolation of patients, individual care and rational treatment;

(2) isolation for 9 days of all persons who have had contact with plague patients and their preventive treatment with streptomycin; if these persons have been administered antiplague serum, their isolation is prolonged to 12 days;

(3) thorough disinsection, deratization, and disinfection of the clothing and other things, as well as the premises in the focus;

(4) house to house canvassing to reveal plague patients and persons who have had contact with them.

An auxiliary role in the prevention of plague is played by inoculations with a living dry vaccine which is dissolved in a sterile physiologic solution directly before administration. The vaccine is administered intracutaneously and epicutaneously (scarifications with Jenner's vaccination lancet). The inoculations confer immunity for a period of one year. Revaccination is performed 6-12 months after vaccination, depending on the epidemiological situation.

The inoculations serve to supplement the measures aimed at liquidating the circumscribed plague focus.

For passive immunization persons who have had contact with plague patients are administered antiplague serum (100 ml subcutaneously).

FOOT-AND-MOUTH DISEASE (APHTHAE EPIZOOTICAE)

The foot-and-mouth disease is an acute zoonotic infection transmitted to man from diseased even-toed animals; it is accompanied by a febrile reaction and development of small vesicles (aphthae) on the oral mucosa, around the mouth and at the nail bed.

Brief historical information. Owing to its characteristic clinical picture, cases of the foot-and-mouth disease among humans and animals have been known since antiquity. The possibility of transmission of the infection from diseased animals to man was demonstrated only at the end of the 18th century. In 1897 Loeffler showed that the causative agent of the disease passes through bacteria-retaining filters.

Aetiology. The causative agent of the disease is a special strain of filtrable virus (*Dermaphilus pecoris*) which parasitizes in the patients' epithelial cells of the oral mucosa and in the skin at the atrium of infection. The virus may spread with the blood flow, which explains the secondary localizations of the causative agent on parts of the mucosa and skin far-removed from the atrium of infection.

Three strains of virus (A, B and C) differing in their antigenic properties are known to cause the foot-and-mouth disease. Their morphological properties have been very well studied with the aid of the electron microscope. The virus is an oval-shaped elementary particle 8-20 μ in size. It is stable in the external environment and resists desiccation (for example, in milk powder) and freezing (in milk).

Epidemiology. Cattle is the main reservoir of the infection in nature, but the disease is also observed among other animals—sheep, goats, camels and hogs.

Young animals are particularly susceptible to the foot-and-mouth disease. The infection is transmitted from diseased animals to healthy animals through common watering places and pastures and as the result of unsanitary maintenance of cattle-yards.

In animals affected with the foot-and-mouth disease the causative agent circulates in the blood and is eliminated in the urine, faeces,

milk and saliva. In infected cows the virus may also be found in the contents of the vesicles appearing on the oral mucosa and on the udder. Animals affected with the foot-and-mouth disease develop numerous vesicles and blisters on the mucous membranes of the mouth, nose, gums, lips and hoofs (hence the designation—foot-and-mouth disease).

Man contracts the foot-and-mouth disease from infected animals mainly through milk (60-65 per cent of all cases).

Less frequently humans contract this disease through direct contact with diseased animals, when the virus gains entrance from the contents of the vesicles, urine and faeces of the animals into the human organism through scratches and abrasions on the skin.

Pathogenesis. The causative agent of the disease penetrates into the damaged oral mucosa and produces the primary affect (small aphtha) at the portal of entry. From the portal of entry the virus passes into the general circulation; this occurs at the very end of the incubation period. With the blood flow the virus comes back to the oral mucosa and causes development of several vesicles (aphthae). The virus brought by the blood flow to the skin settles in the latter and forms vesicles at the base of the nail bed, on the fingers and toes.

An important role in overcoming the infection is played by virucidal antibodies. An attack of the disease confers lasting immunity.

Clinical picture. The incubation period averages about 3 days (it varies between 2 and 6 days); in rare cases it may last up to 10 days. The disease sets in acutely with chills, after which the temperature rises to 38.5-39°C in the course of 3-4 hours. The characteristic complaints of the patients are headache, general jadedness, diminished appetite and muscular pains. Soon the patients develop a burning sensation in the mouth as a result of the pain caused by chewing solid food and formation of vesicles (aphthae) filled with a clear fluid and localized on the oral mucosa (Fig. 71). At the same time the patients begin to salivate copiously.

The temperature is elevated for a period of 5-6 days; small superficial ulcers form at the sites of the initial aphthae. The oral mucosa is inflamed; this is accompanied by copious salivation. At the end of the febrile period the blood shows eosinophilia; moderate leucopenia is less characteristic of the condition. Recovery is accompanied by epithelization of the ulcers on the mucosa.

Diagnosis. To establish the diagnosis, it is necessary to take into consideration the epidemiological data and the clinical picture of the disease. The foot-and-mouth disease is characterized by an acute onset with a sensation of burning and pains in the mouth, especially when chewing solid food, copious salivation, aphthous eruptions on the oral mucosa, the tongue and at the nail bed of the fingers and toes with subsequent ulceration of the vesicles.

Differential diagnosis. The disease must be differentiated from vulgar aphthous stomatitis which quite frequently affects both children and adults. In aphthous stomatitis the vesicles, which are round, become *deeply* ulcerated and the floors of the ulcers are covered with a whitish film, the salivation is less copious than in the foot-and-mouth disease, and there are no eosinophils in the blood.

The diagnosis of the foot-and-mouth disease may be confirmed by infecting guinea pigs, for which purpose the contents of an aphtha are rubbed into the scarified surface of the "cushions" on the feet



Fig. 74. Aphthae on oral mucosa in foot-and-mouth disease

of these animals; typical aphthae subsequently appear at the sites where the contents of the aphthae taken from the patient were rubbed in. Laboratory diagnosis also makes use of the complement fixation test.

Prognosis. Although the foot-and-mouth disease is accompanied by a number of subjective disturbances, it generally runs a favourable course and ends in complete recovery of the patients towards the 15th-20th days from its onset. No lethal results are observed, and a concurrent, secondary infection with development of septic conditions is possible only in debilitated and emaciated children.

Treatment. The patients must be prescribed a sparing diet (semi-liquid, easily assimilable food ingested in divided portions 4-5 times a day). If purulent complications develop in the oral cavity, penicillin injections are administered. Satisfactory results are produced by treatment with novarsenol which is administered intravenously in a dose of 0.3-0.45 g (for adults) at a 48-hour interval (a total of

2 injections). Directly before administration the drug is dissolved in 10 ml of twice-distilled water. It is administered slowly—over a period of 2-3 minutes. Treatment with osarsol (acetarsone) is less effective; this drug is administered per os (0.25 g 4 times per day for 4 days). Favourable results may be produced in individual cases by treatment with biomycin (3,000,000 U 4 times per day for 4-5 days).

The ulcers formed at the sites of aphthae are cauterized with a 4 per cent silver nitrate solution by means of a cotton swab.

To prevent secondary infection, the oral cavity must be repeatedly (3-4 times a day) rinsed with a (1 : 1,000) rivanol (2-ethoxy-6,9-diaminoacridine lactate) solution or a 1 per cent potassium permanganate solution.

Prevention. To prevent the foot-and-mouth disease, no raw milk, or products prepared from raw milk, must be consumed, especially in areas where cases of the foot-and-mouth disease have been observed among cattle. It is necessary to take every precaution, while caring for infected animals, i.e., to wash the hands frequently and wear special clothes—an oilcloth apron, rubber gloves and boots—whenever necessary to contact animals affected with the foot-and-mouth disease.

To control the foot-and-mouth disease among animals, it is necessary to exercise constant veterinary control (reveal and isolate diseased animals, inoculate them against this disease) and to carry out sanitary measures in cattle-yards.

On the cattle farms unfavourable as regards foot-and-mouth disease incidence it is necessary systematically to clean the cattle-yards, make composts, disinfect the cattle-stalls, urinals and feeding-throughs with chloride of lime, and disinfect the manure in the composts. It is strictly prohibited to sell or consume milk from cows affected with the foot-and-mouth disease. Boiling or pasteurization of milk is an important factor in the prevention of the foot-and-mouth disease.

IV.

AIR-BORNE (DROPLET) INFECTIONS

The characteristic epidemiological feature of this group of diseases is that a healthy person becomes infected by a patient on close contact, i.e., the infection is transferred by droplets of moisture containing the causative agent. In coughing, talking and sneezing a patient (or carrier of the infection) excretes into the external environment minutest particles of mucus containing virulent microbes; when these microbes come in contact with the mucous membranes of the upper respiratory tract of a healthy person they may give rise to disease. Many air-borne (or droplet) infections are very contagious and affect large numbers of people who are in contact with patients; this happens, for example, in the case of measles in children's institutions.

Catarrhs of the upper respiratory tract and the nasal mucosa are responsible for the spraying of mucus from the fauces and nasopharynx during talking, coughing and sneezing with the result that nearby healthy persons may become infected. The incidence of air-borne infections often increases during the cold time of the year owing to the frequency of catarrhal changes in the nasopharynx and upper respiratory tract.

The causative agents of air-borne infections may be bacteria (diphtheria, whooping cough) and filtrable viruses (smallpox, influenza). Some air-borne infections may result in bacteria-carrying, as is sometimes the case in diphtheria.

CHICKENPOX (VARICELLA)

Chickenpox caused by a filtrable virus is an acute infectious disease of children; it is accompanied by a febrile reaction and a characteristic vesicular eruption all over the skin.

Actiology. The disease is caused by a special strain of filtrable virus (*Strongyloplasma varicellae*) which is found mainly in that fluid of the vesicles appearing on the patient's skin; it is present in the vesicles during the period of "flourishing" of the eruption

*

and disappears by the time the crusts fall off. Virusaemia—circulation of the virus in the blood—is also observed.

The virus is unstable in the external environment and is quickly destroyed by desiccation.

Epidemiology. Chickenpox is a rather widespread disease mainly of younger children, although now and then it occurs in youths. Patients—from the onset of the febrile period till the falling-off of the crusts—are the only source of the infection.

By one of its symptoms (vesicular eruption on the skin) chickenpox somewhat resembles smallpox, but it differs from the latter disease completely in its aetiology, immunology, most important clinical manifestations, favourable course and prognosis.

Chickenpox is transmitted through the *air* (at the end of the incubation period and during the first 3-4 days of the eruption) and by *contact* (during later periods of the disease). Chickenpox patients are very contagious, especially during the early period of the disease. All children living in one apartment or hostel with rooms connected by a common corridor must be considered infected with chickenpox even if only one child has fallen ill. This similarly applies to nurseries and kindergartens where a quarantine must be established for 21 days upon the appearance of even one sick child.

An attack of the disease confers lifelong immunity.

Clinical picture. The incubation period averages 15-17 days (and may vary between 11 and 21 days). There are hardly any prodromal symptoms.

In individual, rather rare cases a prodromal eruption may appear: it looks like a scarlet fever rash. The eruption does not have a favourite localization, may spread all over the body and lasts for several hours. Sometimes the prodromal eruption may appear in the presence of the true chickenpox eruption.

Soon after the rise in temperature (38-39 C) a rather abundant eruption in the form of small (1-3 mm in diameter) round rose-coloured macules appears on various parts of the skin and mucous membranes, mainly of the nasopharynx and the fauces. Subsequently the eruption undergoes a transformation: in a very few hours the rose-coloured macules change to vesicles filled with a clear liquid. A narrow red inflammatory rim forms along the periphery of individual vesicles. Some of the vesicles are pitted in the centre, which increases the purely external resemblance to the smallpox eruption.

During the days immediately following, an additional eruption of rosecolous elements breaks out on the skin of the chickenpox patient, these elements soon changing to vesicles. It should be remembered that in chickenpox many vesicles dry up or burst the day after their appearance, or the patient scratches them so that crusts are formed in their place. The eruption is characteristic for

its *polymorphism*, i.e., simultaneously with fresh elements there are burst vesicles and even dry crusts on the skin.

During the first 6-7 days of the disease vesicles may repeatedly break out in spurts. At the end of this period the temperature returns to normal. The contents of some of the vesicles grow turbid before the vesicles burst. The vesicles forming on the mucous membranes of the mouth, pharynx and larynx and on the conjunctivae of the eyelids may easily ulcerate, which makes possible the penetration of secondary infection with development of septic processes. It is therefore necessary strictly to observe personal hygiene.

The blood picture is scarcely characteristic; it usually exhibits but mild leucopenia.

In most cases chickenpox runs a favourable course, and lethal results are but extremely rarely observed. In young children with nutritional disorders (malnourished, undernourished) or with a mixed infection (diphtheria, scarlet fever, measles) chickenpox may considerably aggravate the prognosis. In such children suppuration of the skin eruption with development of abscesses, phlegmons and sepsis is possible. The presence of numerous vesicles on the mucous membranes of the upper respiratory tract may serve as the cause of laryngeal oedema.

In favourable cases the disease lasts a total of about 20 days (until the crusts have fallen off).

In cases where the disease **runs** a normal course and in children who have been given **gamma-globulin** or antimeasles serum for preventive purposes, *atypical* forms with mild skin eruptions may be observed.

Several variants of a more severe, although rare, course of the disease, mainly in emaciated 2-6-year-old children, are known.

In most cases chickenpox exhibits a characteristic clinical picture, but the following forms of the disease are also possible.

1. *Pustular form*. In this form the contents of the vesicles become purulent, the vesicles not infrequently contain blood, the centre of the vesicles is pitted and an annular infiltrate appears around them. As the burst pustules dry, sanguineous crusts are formed; the crusts fall off only in the fourth week of the disease. Such cases greatly resemble smallpox, and it is therefore particularly necessary carefully to differentiate this disease from smallpox (see "Smallpox").

2. *Bullous form*. This form is rare; large blisters filled with a clear fluid form on the skin.

3. *Gangrenous form*. In cases of a sharply lowered general resistance of the organism due to avitaminosis and alimentary dystrophy a gangrenous form of chickenpox may be observed. In these cases a number of vesicles enlarge and fill with a pyosanguineous fluid; an inflammatory (hyperaemic) zone appears around individual vesicles. Then the vesicles burst and necrotic scabs form in their

place. Disengagement of the scabs exposes deep and long-unhealing ulcers. The gangrenous form of chickenpox runs a severe course and may become complicated by septicopyemia.

4. *Haemorrhagic form.* In some cases the vesicles on the skin may fill with a haemorrhagic content, while multiple petechiae form on some parts of the skin free from the eruption. The development of the haemorrhagic form of chickenpox is usually accompanied by septic complications.

An attack of chickenpox confers stable immunity.

Diagnosis and differential diagnosis. The characteristic temperature reaction retained to the end of the eruption, the successive transformations of the eruption elements with new eruptions repeatedly breaking out on the skin in spurts, simultaneous presence of various phases of development of vesicles, and leucopenia in the blood considerably facilitate the diagnosis of typical cases of chickenpox.

Differential diagnosis. The disease must be differentiated from smallpox mainly in cases of its pustular form and in the event of epidemiological indications that smallpox may have been brought into the given area.

In differentiating the disease from smallpox it is primarily necessary to ascertain the epidemiologic data, including (a) whether or not the given patient had any contact with smallpox or chickenpox patients for 22 days preceding the onset of the disease, (b) whether or not the patient has ever had smallpox or chickenpox, and (c) whether or not the patient was vaccinated and revaccinated against smallpox for 3 years preceding the onset of the disease, with a positive skin reaction at the site of the vaccination indicating the absence of immunity to this disease.

Following this the patient must be carefully examined and all available clinical data must be considered.

It is necessary to take into account that in chickenpox patients prodromal phenomena are either absent or are feebly marked and show no peculiarities; the temperature is elevated till the end of the eruption period which lasts 6-7 days; the small vesicles, filled with a clear fluid, on the skin and mucous membranes are at different stages of development (polymorphism of the eruption); the blood exhibits leucopenia; the fluid in the vesicles contains a number of giant multinucleate cells well seen in stained preparations under the microscope. Chickenpox usually runs a favourable course.

In cases of smallpox the patient's condition is quite serious already during the prodromal period, the general phenomena are strongly pronounced, the temperature is high, and there is a characteristic roseolous-petechial eruption in femoral triangle and in the brachial triangle. In the beginning of the eruption the temperature falls and then rises again at the time of pustulation. Small-

pox vesicles are multichambered and do not collapse when punctured with a sterile needle.

It should be remembered that in smallpox the eruption is monomorphous and that it localizes mainly on distal parts of the body (forehead, hands); the eruption lesions have a compact base (see Differential-Diagnosis Table in "Smallpox").

Epidemiological data play an important role in the establishment of the diagnosis.

In cases of the least suspicion of smallpox, especially if the epidemiological data make this disease quite probable, and if it is impossible to establish a sufficiently reliable differential diagnosis, it is necessary to carry out the anti-epidemic measures required by the appearance of smallpox.

Treatment. Chickenpox patients are usually isolated at home and only severe cases are hospitalized.

The skin eruptions are painted with a 1 per cent alcohol solution of methylene blue; in cases of intense itching it is necessary to paint the skin with a 5 per cent alcohol solution of menthol. In the pustular and gangrenous forms of the disease the patients must be given penicillin injections.

Prognosis. Typical cases of chickenpox run a favourable course. In severe cases of this disease in debilitated children and in cases where chickenpox is combined with other infectious diseases the prognosis is often serious.

Prevention. On the appearance of a case of chickenpox in nurseries or kindergartens a 21-day quarantine is established. Children who never had chickenpox, but at the given time had contact with a patient, are excluded from children's institutions for the same period of time. In cases of mixed infection (for example, chickenpox and measles) patients must be hospitalized and placed in separate compartments.

Children who had any contact with a chickenpox patient are prophylactically administered antimeasles serum (50 ml) or gamma-globulin (2-3 ml). Patients kept at home must be isolated as much as possible from children who never had chickenpox.

INFLUENZA

Influenza is an acute infectious disease caused by a filtrable virus of various serological types and characterized by symptoms of general intoxication. The disease produces a number of disturbances in the activities of the nervous and cardiovascular systems and is accompanied by a short febrile period often with affections of the mucous membranes of the upper respiratory tract. Influenza may occur as single cases and as widespread epidemics.

Brief historical information. Human diseases with the clinical picture of modern influenza were known to physicians even in antiquity. Extensive epidemics of influenza, often assuming the character of pandemics, have been repeatedly described since the 12th century.

Four influenza pandemics were observed in Europe in the course of the 19th century (1830-1833, 1836-1837, 1847-1848, 1889-1890).

The 1918-1920 influenza pandemic assumed tremendous proportions for it affected countries not only in Europe and America, but also on the other continents. During this pandemic exceptionally severe cases of influenza took a toll of many human lives; subsequently cases of influenza ran a much more favourable course.

In 1957 there was another influenza pandemic; the disease was caused by type A₂ virus. Outbreaks of influenza caused by the same virus were observed in a number of communities in the beginning of 1959.

In 1933-1934 it was demonstrated that influenza is caused by a filtrable virus and the disease was experimentally produced in polecats. Later mice and white rats were used as an experimental model for the infection. Research in virology, immunity and laboratory diagnosis of influenza, as well as elaboration of methods of active immunization against the disease, has assumed wide scope since 1942. The problem of influenza was given all-round consideration in the studies of Soviet scientists; however, improvement of laboratory diagnosis of the disease and of its specific prevention by inoculation with living vaccines continues to be the immediate task of the investigators.

Aetiology. Influenza is caused by a filtrable virus (*Pneumophylus gripposus*) of several serologic types (A, A₁, A₂, B, C and D); the most is now known about types A, A₁, A₂, (A_{ASL} or A₅₇) and B. Some authors consider types C and D virus as belonging to the causative agents of parainfluenzal diseases. The clinical picture of influenza produced by all of these types is largely the same, except certain peculiarities depending on the biologic properties of each particular type.

Today the predominant type of influenza virus circulating between patients and healthy (disease contracting) people is type A₂.

The extremely severe clinical course of influenza during the 1918-1919 pandemic was apparently due to the high virulence of the causative agent—passage virus which turned out to be highly adapted to the human organism during its continued transmission from patients to healthy people under epidemic conditions.

The causative agent of influenza parasitizes in the epithelial cells of the upper respiratory tract, liberating in the process of its metabolism and disintegration toxic substances which are responsible for the general intoxication of the organism.

The influenza virus is represented by spherical elementary particles well seen under the electron microscope when magnified 40,000-60,000 times.

The virus may be cultivated in the pulmonary tissue of white mice or on the chorioallantois of the chick embryo. By centrifuging it it is possible to obtain a pure culture of the virus pathogenic not

only to man, but also to certain laboratory animals (white mice, white rats, polecats).

Virus-neutralizing antibodies circulating in the blood accumulate in the patient's organism; the blood serum of people who have survived an attack of influenza is also capable of inhibiting the agglutination reaction.

In the external environment the influenza virus quite rapidly disintegrates under the action of sunlight, heat (above 30°C) and disinfectants, and as a result of desiccation. In the mucus sprayed from the patient's nasopharynx during sneezing and coughing the virus retains its viability for quite a long time.

Detailed studies of the properties of the virus of various strains and serologic types have made it possible to reveal a number of epidemiologic peculiarities of influenzal infection. It was found, for example, that the inadequate immunity conferred by an attack of influenza is due to the variability of its causative agent.

Epidemiology. Patients are the only source of infection in all cases; they are particularly contagious during the first 1-2 days of the disease.

While coughing, sneezing and talking a patient sprays into the air and on various objects minutest droplets of mucus containing the influenza virus, thereby spreading the disease since influenza is an *air-borne* infection. The transmission of the infection is favoured by close contact between patients and healthy susceptible people. Influenza occurs as single cases and as epidemics. The contacts of people in everyday life, on the transport and at work create extensive possibilities for spreading the infection. On coming in contact with the mucous membranes of the fauces, nose and upper respiratory tract of a healthy person the influenza virus penetrates through the mucous membranes, enters the general circulation and produces the disease.

The effective measures of controlling influenza today consist only in personal prophylaxis, sanitation, and isolation of influenza patients.

An attack of influenza does not confer adequate immunity, especially since the various strains of the same or different types of virus (A, A₁, A₂ and B) do not produce cross immunity in those who have survived an attack of the disease; recurrent attacks of influenza in the course of the same year are possible.

It should be remembered that the factors favouring infection with influenza include cooling, upper respiratory catarrhs which facilitate the penetration of the virus, and vigorous activity of the pathogenic bacterial flora usually present in the oral and nasal cavities and on the mucous membranes of the trachea and bronchi. The foregoing harmful factors lower the general resistance of the human organism and, on sufficiently close contact of a healthy person with an influenza patient, facilitate infection with the in-

fluenza virus. However, the role played by the foregoing factors in increasing the susceptibility to the disease must not be overestimated because influenza cases may be observed not only during the cold and damp time of the year, but also in summer. True, epidemic outbreaks in the moderate climate zone usually occur in autumn and winter, and especially frequently in early spring (March-April).

It has been established by virological studies that of the influenza epidemics observed in the USSR in recent years the one in the spring of 1949 was caused by type A virus, the one in the autumn of 1949—by type B virus, the epidemic of February-March 1952—by type A₁ virus, and the 1957 and 1959 epidemics—by type A₂ virus.

The regular feature in the appearance and development of influenza epidemics is that the highest incidence of the disease is observed 15-20 days after the outbreak of the epidemic and that the incidence subsequently gradually decreases. The epidemic outbreak lasts a total of 2-2.5 months. Outside the epidemics the cases of influenza are sporadic.

Pathogenesis and pathologic anatomy. After gaining entrance into the human organism through the upper respiratory tract the influenza virus attacks the mucous membranes of the fauces, nasopharynx and trachea, and then lodges in the epithelial cells lining the upper respiratory tract. Soon the causative agent begins to circulate in the blood, but virusaemia is not an essential part of the pathogenesis of influenza and lasts but a short time. The main manifestations of the disease are associated with the effects produced by the toxic products of the filtrable virus on the nervous and cardiovascular systems (disorders of their functions) and on metabolism (disturbances in metabolic processes).

Influenza now runs a rather favourable course and lethal cases are quite rare, but we must not overlook the possibility of death as the result of severe toxic forms of influenza or concurrent complications.

Pathoanatomic examinations of corpses of people who have died of influenza reveal a picture of acutest catarrhal laryngotracheitis which, in some cases, is of a fibrinous-haemorrhagic character. Pathohistological observations show marked degeneration of cells in various organs (including the central and peripheral nervous system) and necroses in the liver, spleen and lymph nodes. Cases of influenza complicated by pulmonary pathology reveal numerous foci of serous-haemorrhagic, confluent or fibrinous-haemorrhagic pneumonia.

The extremely severe clinical course of influenza during the 1918-1919 pandemic was characterized by development of catarrhal-haemorrhagic and fibrinous-haemorrhagic bronchitides and bronchiolitides, extensive haemorrhagic pneumoniae, haemorrhagic encephalitis and acute interstitial myocarditis.

Clinical picture. The incubation period of influenza averages 1-2 days, but may be from 12 hours to 3 days. We shall examine the usual course of the disease first.

Uncomplicated influenza sets in acutely with marked intoxication and a short (2-3 days) febrile period.

The disease begins with chills followed by a rapid rise in temperature which reaches 38.7-39.8°C during the first 4-5 hours. The patient's condition changes very much for the worse; the patient is discomforted by headache, especially in the region of the forehead and the supraorbital arches, general weakness, jadedness, pains in the joints, dizziness and tinnitus.

The initial period of influenza is characterized by a sensation of dryness, "scratching" pains in the fauces, pharynx and larynx (laryngitis). Soon afterwards pains appear in the eyeballs; these pains are particularly intense upon abduction of the eyes. Olfaction is diminished, while auditory and visual acuity is, on the contrary, increased. Some patients exhibit conjunctivitis, lacrimation, rhinitis and dry coughing. The appetite is usually diminished and the stool is retained. The neuropsychic state is marked by irritability and considerable excitability of influenza patients.

Examination of influenza patients reveals hyperaemia of the skin of the face and of the conjunctivae. The respiratory rate is increased, the blood pressure is somewhat lowered, and the pulse rate usually lags behind the temperature level (relative bradycardia); sometimes the pulse is arrhythmic (extrasystoles). The heart sounds are dull. In severe cases the percussion borders of the heart are observed to be extended (usually to the right) and the apical sounds to be very dull; sometimes a blowing systolic murmur associated with phenomena of myocardial dystrophy is auscultated.

Although mainly small blood vessels suffer changes in influenza, clinical and electrocardiographic data often attest the involvement of the myocardium in the pathologic process with development of marked dystrophic changes caused by intoxication. Development of severe myocarditis is sometimes observed.

Capillaroscopy reveals circulatory disorders in the arterio-capillary system.

The clinical picture of influenza abounds in neurologic symptoms. In some patients, especially in severe toxic forms of the disease, these symptoms may be particularly strongly pronounced due to the development of meningoencephalitis, encephalomyelitis, myeloradiculitis and peripheral neuritides.

The tongue is dry and its root is coated with a white film; the mucosa of the lips often shows cracks. The liver and spleen are usually not enlarged.

In uncomplicated influenza the febrile period averages 2-3 days (Fig. 75), rarely lasting 5 days or only 1 day. At the end of the

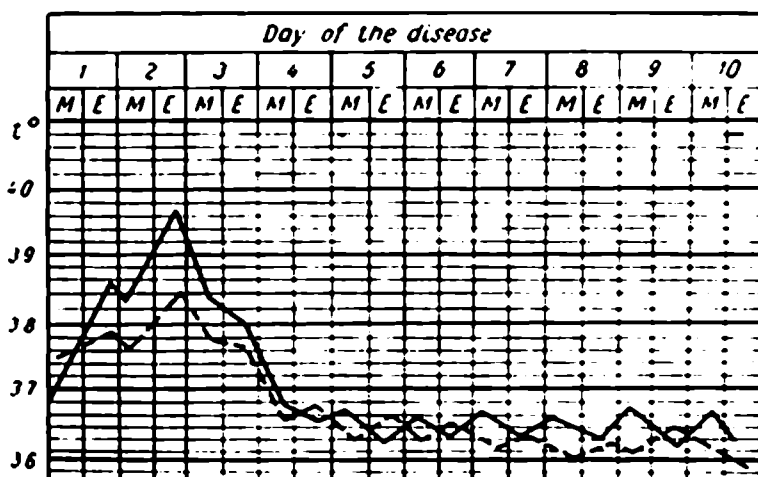


Fig. 75. Temperature curve of patient with uncomplicated influenza.

febrile period the temperature falls to normal critically or by accelerated lysis.

If the febrile period of the disease whose diagnosis is not clear lasts more than 6 days, either the diagnosis of influenza is wrong or it is a matter of some complication. Primary influenzal pneumonia should be remembered.

Sometimes a saddleback temperature curve is observed: on the second or third day of the febrile period the temperature falls to normal, but 24-36 hours later rises again, the febrile period lasting a total of 6-7 days.

Blood tests of influenza patients show leucopenia (up to 3,000-3,500 leucocytes per 1 cu mm), aneosinophilia, relative lymphocytosis, a shift of the neutrophilic series to the left, and a moderately accelerated ESR (an average of 20-22 mm/hr).

The following three basic forms of uncomplicated influenza are distinguished according to their course: (1) mild, (2) moderately severe and (3) severe (toxic).

In addition to the afore-described typical clinical form of influenza there are *atypical* and *effaced* forms of the disease. Although these cases run a mild course, and the pathologic symptoms are feebly marked and quickly liquidated, they are of very great epidemiological importance as sources of infection. Unidentified these cases may contribute to a further spread of the disease.

Severe, *toxic* forms of influenza are marked by extreme intoxication of the organism and predominant affection of the nervous and cardiovascular systems; such cases are often accompanied by haemorrhagic phenomena on the skin and mucous membranes and nasal haemorrhages. These severe forms of the disease are dangerous to life.

In typical cases the normalization of the temperature is rapidly followed by improvement in the patient's general condition, better appetite, and normal, undisturbed sleep.

Complications. The most characteristic complications of influenza include influenzal and staphylococcal focal pneumoniae, otitides, ethmoiditides, highmoritides and frontitides.

Influenzal pneumoniae are characterized by microfocal affections of pulmonary tissue (usually posteroinferior parts of the lungs) revealed by percussion and auscultation. The blood picture exhibits leucocytosis, a neutrophilic shift of the leucocytes to the left and a considerable acceleration of the ESR.

Some patients develop neuritides of the cranial nerves and the brachial plexus, and stable ischialgias. Meningoencephalitides and myeloradiculitides occur much less frequently. The cardiovascular system may be affected with thrombophlebitides and myocarditides.

Severe cases of influenza may be accompanied by acute vascular insufficiency (collapse). Complications considerably aggravate the prognosis and may serve as the cause of death, especially in severe cases.

Influenza does not confer stable immunity, hence the frequent recurrence of its attacks.

Prognosis. In cases of moderately severe and in mild forms of influenza the prognosis is usually favourable, especially if the patient is kept in bed.

In severe (toxic) forms of the disease the prognosis is doubtful.

Complications not only prolong the disease and inflict a good deal of suffering on the patient, but may also serve as the cause of death, especially in persons of advanced age and infants, and in cases of alimentary emaciation, avitaminoses and chronic diseases of the heart, liver and kidneys. Influenza may activate old, already extinguished pulmonary tuberculosis and give rise to complications caused by staphylococci and streptococci present on the mucous membranes of the upper respiratory tract.

Diagnosis. During influenza epidemics the disease is not difficult to diagnose because of its mass spread and the characteristic clinical picture in most of the patients; it is quite difficult to diagnose during the periods intervening between the epidemics.

The diagnosis of influenza is established on the basis of such symptoms as an acute onset with a rapid rise in temperature, headache felt mainly in the forehead and supraorbital arches, conjunctivitis, pains on moving the eyes, general intoxication, jadedness, pains and a "tickling" in the throat (pharyngitis), dry cough, relative bradycardia and characteristic changes in the blood picture (leucopenia with aneosinophilia, relative lymphocytosis and neutrophilic shift to the left). It is very often necessary to *differentiate* influenza from so-called acute viral respiratory diseases caused mainly

by adenoviruses. These diseases usually occur at the cold time of the year and have a clinical picture which greatly resembles that of influenza. The most important differences between these diseases and influenza are that the former are very definitely due to a general cooling of the organism, their onset is usually rather gradual (the temperature rising to high figures over a period of 1.5-2 days), the catarrhal phenomena (rhinitis, coughing with a plentiful discharge of mucopurulent sputum) are observed in all cases and are strongly pronounced, while the headache and general intoxication of the organism are negligible; the blood picture shows no characteristic features. However, precise differentiation is very difficult.

In establishing a differential diagnosis it is also necessary to consider such infectious diseases as *typhus* and *marsh fever* (Table 5), as well as *pappataci fever* which is an endemic disease.

No methods of laboratory diagnosis of influenza satisfactory to medical practice have as yet been elaborated. That is why only the most general information on laboratory examinations suggested for the diagnosis of influenza is given below.

The blood serum of people affected with influenza retards the reaction of a haemagglutination (clumping of erythrocytes of the guinea pig by means of particles of the influenza virus); this "inhibition test" is very sensitive and specific; it may serve to confirm the diagnosis, but it cannot be performed before the 14th or 16th day of the disease and can therefore only confirm the diagnosis of an already survived attack of influenza.

Only specially equipped laboratories are capable of determining the virus-neutralizing antibodies in the blood of influenza patients and isolating the virus from an irrigation of the nasopharynx.

Treatment. Influenza patients are treated at home. Only in severe and complicated cases are influenza patients placed in contagious hospitals or contagious divisions of hospitals.

Bed rest is necessary for the entire febrile period. Patients who have survived an attack of influenza must not be allowed outdoors before two days have elapsed since the normalization of temperature. The periods of temporary disability for influenza patients are determined strictly individually.

Influenza patients are placed in warm, light and well-ventilated rooms (or wards). To isolate the patients from each other, their beds are screened by a sheet or screen (see Fig. 14). The patient's room must be frequently aired, but so as not to chill the patient.

The patient must be wrapped up warmly, with heat (hot water bottles) applied to his feet, and must be given plenty of hot drinks (milk, strong sweet tea with lemon and preserves or jam, coffee and cocoa). The diet must consist of easily-assimilable, high-calory, various and vitamin-rich foods.

The persons caring for the patient must wash their hands with hot water and soap and wear gauze masks covering the mouth and nose.

Table 5

Table of Differential Diagnosis of Influenza, Typhus and Marsh Fever

Symptom	Influenza	Typhus	Marsh fever
Onset of the disease and character of the temperature curve	Acute; temperature rises to 38.5-40°C in a few hours; in some patients the rise in temperature is preceded by chills. The febrile period most commonly lasts 2-3 days, but now and then may be 5-6 days. A saddleback temperature curve is possible	Acute or subacute. In 24-48 hours the temperature usually rises to 38.8-40°C and persists at this level for several days. It falls by an accelerated lysis; the fever lasts a total of 10-12 days	Acute; chills towards the end of the first day of the disease; temperature rises to 39-39.5°C, persists at high figures for 6-8 days and then falls to normal by accelerated lysis. After 3-4 days of apyrexia a temporary (for 1-2 days) relapse of the disease is possible
Patients' complaints	Headache, general weakness, jadedness, pain in the region of the supraorbital arches and on movement of the eyes; a "full and stuffy" feeling behind the sternum. In some cases—insomnia and anorexia	Sharp, continuous headache, insomnia, jadedness, loss of appetite	General weakness, mild headache, jadedness
Consciousness	As a rule retained, except in hypertoxic cases	In severe cases it is circumscribed or clouded. Delirium and excitement are possible	Usually clear all through the febrile period of the disease
Headache	Characteristic: pain localized in the forehead and region of supraorbital arches	Sharp, involving all of the head	Often observed, involves all of the head, mild
Pain upon pressure on the eyeball	Characteristic	Absent	Inconstant sign

Pain in gastrocnemius muscles	Not characteristic	Not characteristic	Typical, occurs in many patients
Rhinitis and cough	Far from constant, but occurs in a number of patients	Absent	Absent
Conjunctivitis	Same	Absent, but conjunctival vessels are injected	Often observed
Petechiae on conjunctivae (Chiari-Avitsyn sign)	Absent	Observed in a number of patients (especially after instillation of 1 : 1,000 adrenalin solution)	Absent
Herpetic eruptions	Observed in some patients	Not characteristic	Not characteristic
Appearance of the patient's face	Often hypernemic, some cases are accompanied by conjunctivitis	Not only hypernemic, but also puffy. Red "rabbit" eyes due to injection of vessels of the sclerae and conjunctivae	Often hyperaemic. Vessels of sclerae and conjunctivae injected; conjunctivitis observed
Changes in the fauces	Diffuse hyperaemia	Enanthema at the root of the uvula and on the soft palate is observed on the 3rd-4th days of the disease	Not characteristic, sometimes mild hyperaemia of the tonsils
Nasal haemorrhages	Very rare	Observed only in haemorrhagic forms	Occur in 25-30 per cent of the cases
Skin eruptions	Absent	Characterized by polymorphous roseolous or roseolous-petechial eruption breaking out on the 4th-5th days with favourite localization	A maculopapular, roseolous-petechial or petechial eruption localized on the skin of the chest and abdomen appears between the 4th and 6th days of the disease in 20-25 per cent of the patients and lasts 1-4 days

Symptom	Influenza	Typhus	Marsh fever
Symptoms of capillaropathy (tourniquet, pinch, and cup)	Possible only in toxic cases	Observed in some patients	Possible only in individual patients
Enlarged liver	Absent	Enlarges between the 4th and 6th days of the disease	Enlarged from the 3rd or 4th day of the disease in most patients
Enlarged spleen	Absent	Enlarges between the 3rd and 5th days of the disease	Enlarges only in half the cases from the 3rd or 4th day of the disease
Blood picture	From the second day of the disease — leucopenia, neutropenia (sometimes with a moderate shift to the left), relative lymphocytosis, eosinopenia, ESR accelerated to 18-20 mm/hr	Becomes characteristic from the 3rd day of the disease: moderate leucocytosis, neutrophilia with a shift to the left, lymphocytopenia, eosinopenia; ESR accelerated to 16-18 mm/hr. In 20-25 per cent of the cases — normocytosis; in 10 per cent of the cases — moderate leucopenia	From the 2nd-3rd day of the disease — moderate leucocytosis (8,000-9,000 leucocytes per 1mm ³) with some nuclear shift to the left

The patient must be provided with individual dishes which must be sterilized by boiling after the meals.

In cases accompanied by headaches and neuritides the patients are given analgesics—analgin (1-phenyl-2, 3-dimethyl-5-pyrazolone-4-methylaminoethylene sodium sulphate), pyramidon and phenacetin (acetophenetidin). Patients afflicted with insomnia are prescribed medinal (barbital sodium), luminal, sonbutal (butallylonal), barbamyl (amytal sodium); in cases of a persistent dry cough patients are administered codeine. Patients with marked cardiovascular disturbances are given injections of cordiamine, ephedrine and camphor; in other cases it suffices to administer caffeine per os.

No specific treatment of influenza has as yet been elaborated. Antibiotics and drugs are administered in cases accompanied by complications with pneumonia, otitis and sinusitides. The agents used on strictly individual indications are penicillin, albomycin (antibiotic isolated from *Actinomyces subtropicus*), streptomycin, ecmonovocillin, levomycetin and norsulphazol. In severe cases and to extremely debilitated patients these agents, especially penicillin, may be administered from the very first or second day of the disease to prevent purulent complications and pneumoniae. In a number of cases a favourable effect is produced by aerosols of A. A. Smorodintsev's anti-influenza serum sprayed by a special apparatus; the treatment is administered according to special instructions, the average single dose for application to the nasal mucosa being 0.15 g of dry serum.

The blood serum of convalescents may be administered intramuscularly for the treatment of children affected with influenza.

Prevention. Patients with severe forms of influenza must be placed in contagious hospitals (departments). Patients kept at home must be isolated from the rest of the people at least by a screen; current disinfection must be carried out by the moist method. It is absolutely obligatory for every patient to wear a gauze mask, use handkerchiefs when coughing and sneezing, and have individual dishes. A mother affected with influenza must also wear a gauze mask when nursing her baby. The people in the patient's family or apartment must take measures of personal precaution (wear gauze masks).

A quarantine must be established in all children's institutions—nurseries, kindergartens, children's homes and, if possible, in schools for the duration of the epidemic. During this period no visits to patients in hospitals must be permitted.

To prevent influenza, residential and production buildings, as well as children's institutions, must be systematically ventilated and irradiated by means of mercury vapour lamps. The population must be instructed in ways and means of personal influenza prevention.

Living vaccines from a pure culture of the causative agent of influenza have now been developed for inoculations against the disease.

DIPHTHERIA

Diphtheria is an acute general infectious disease transmitted through the air and caused by a diphtheritic bacillus which produces a strong exotoxin. The disease is accompanied by marked intoxication of the organism and a fibrinous inflammation at the atrium of infection (fauces, larynx, trachea, eye, skin).

Brief historical information. Diphtheria which was known as a separate disease entity already in antiquity began to be studied scientifically by the French clinician Bretonneau in 1826. On the suggestion of Bretonneau and his pupil Trousseau the disease was named "diphtheria" from the Greek word *diphthero* meaning leather and membrane; this term characterizing one of the most typical signs of this disease—formation of films or membranes in the patient's fauces—is still used today.

The causative agent of the disease—diphtheritic bacillus (*Corynebacterium diphtheriae*)—was discovered by Klebs in 1883 and was studied in detail in cultures by Loeffler in 1884. Soon afterwards Roux and Yersin isolated the exotoxin produced by the diphtheritic bacilli; an antitoxic antidiphtheritic serum was produced in 1894 and was subsequently used in the treatment of diphtheria. In Russia diphtheria began to be treated with serum in 1894 (G. N. Gabrichevsky).

To reveal human susceptibility to diphtheria, Schick proposed a skin test with diphtheritic toxin in 1912. Active human immunization against diphtheria by means of anatoxin (i.e., toxin treated with formalin) by Ramon's method has been practised since 1913.

Aetiology. The causative agent of the disease is a bacillus averaging $2-3\mu$ in length and 0.5μ in thickness; it is somewhat curved and has inflations at its ends. The inflations contain special inclusions—Babes-Ernst bodies revealed by Neisser's stain. Diphtheritic bacilli are nonmotile, do not form spores, stain well with fuchsin and are gram-positive.

In cultures the *B. diphtheriae* arrange themselves in groups in the form of fingers of an open hand. The cultures develop well in coagulated horse or ox serum. Eliminated into the external environment in the mucus from the fauces or in the fibrinous membranes the diphtheritic bacilli may long remain viable (2-3 weeks), resist desiccation and retain their virulence under the action of weak disinfectants.

Three varieties of diphtheritic bacteria are distinguished according to their virulence: *gravis* (causes the severest forms of the disease), *mitis* (causes mild forms of diphtheria), and *intermedius* (intermediate variety). It should be noted that there is no direct parallel between the variety of causative agent and the severity of the clinical manifestations of the disease it causes. It is now possible to determine the toxigenicity of the strains of bacteria isolated from patients by a precipitation test in agar.

Diphtheritic bacteria eliminate into the surrounding medium a strong exotoxin of complex protein nature. Treatment of the exotoxin with a formalin solution produces an *anatoxin* which has no toxic properties, but possesses antigenic ability; this ability forms the basis of inoculations against diphtheria.

To reveal human susceptibility to diphtheria (or rather immunity to diphtheria), the Schick test is used, namely, one-fiftieth MLD (minimum lethal dose) is injected intracutaneously into the forearm. In positive cases, i. e., if the subject is susceptible to diphtheria, hyperaemia and a swelling 1.5-3 cm in diameter can be seen on the skin 48 hours after the injection.

Epidemiology. Diphtheria patients and bacteria carriers are the source of diphtheritic infection. The disease most commonly attacks children, especially 2-11 years old. Diphtheria is an air-borne infection; by coughing or sneezing the diphtheria patient or bacteria carrier discharges into the air minutest particles of mucus containing virulent diphtheritic bacteria. The infection takes place when these particles gain entrance into the nasopharynx and upper respiratory tract of a nearby healthy susceptible person.

The disease develops much less frequently when diphtheritic bacteria come in contact with the conjunctiva of the eye or penetrate into a wound on the surface of the skin.

A certain role in spreading the infection is played by various household articles and toys infected with particles of mucus from the fauces of patients or bacteria carriers.

Diphtheria incidence is clearly seasonal; it increases in late autumn and the beginning of winter because of the frequency of catarrhal processes in the nasopharynx and upper respiratory tract of carriers at this time of the year with the result that more particles of mucus containing virulent bacteria are sprayed during coughing and sneezing. At the same time nasopharyngeal and upper respiratory catarrhs in otherwise healthy susceptible people facilitate infection with diphtheria. Cases of diphtheria now occur in the USSR mainly sporadically.

An attack of the disease does not confirm adequate immunity, owing to which reinfection is possible. In some cases people who have recovered from diphtheria become temporary or chronic bacteria carriers. Susceptibility to bacteria depends on age; infants up to 1 year of age are barely susceptible; subsequently susceptibility rapidly increases and reaches its maximum between 3 and 11 years of age. Adults are affected with diphtheria much less frequently than children.

Pathogenesis and pathologic anatomy. Faucial diphtheria is the most frequent form of the disease, the causative agent producing a number of pathologic changes at the atrium of infection (tonsils, palatine arches and the uvula).

In addition to this most common localization of the diphtheritic process there are other varieties of the disease—nasal diphtheria, laryngeal diphtheria and, much less frequently, ocular diphtheria and cutaneous diphtheria.

The pathoanatomic changes at the atrium of infection are characterized by development of a fibrinous (diphtheritic) inflammation and

formation of dirtyish-white or ash-grey membranes which closely adhere to the underlying tissue. These membranes consist of a tremendous number of fibrinous threads with leucocytes and desquamated epithelium of the mucous membrane; the membranes contain virulent diphtheritic bacteria. Owing to the close adhesion of the fibrinous threads to the underlying tissues the membranes can hardly be separated from these tissues with a cotton tampon or spatula. Diphtheritic films on the mucosa of the trachea and bronchi are loosely connected with the underlying tissues. As the patient recovers the number of membranes decreases, exposing easily healing superficial ulcers. Nasal diphtheria is accompanied by a sanious discharge from the mucous membrane.

However, the pathogenesis of diphtheria is not confined to the foregoing local changes at the atrium of infection. Some of the most important clinical manifestations of the disease are due to the fact that from the atrium of infection the exotoxin produced by the diphtheritic bacteria is absorbed and various degrees of intoxication develop.

The toxicoses result in affections of the peripheral nerves (to the point of development of paralyses and disintegration of the myelin sheath) and ganglia of the sympathetic and parasympathetic nervous systems, myocardial dystrophy and, in severe (toxic) forms of the disease, development of progressive myocarditis, degeneration of the adrenals and marked arterial hypotension. Degeneration of parenchymatous organs (liver, kidneys) is observed in the process of the disease. Toxic forms of the disease are characterized by oedema of the subcutaneous tissue at the atrium of infection. For example, the toxic form of faucial diphtheria results in massive oedema of the subcutaneous tissue of the neck. Laryngeal diphtheria is accompanied by oedema of the vocal folds and laboured respiration.

Clinical picture. The incubation period of faucial diphtheria averages 4-7 days, but may be from 2 to 10 days.

The primary focus of affection (i. e., the atrium of infection) determines the following varieties of clinical forms of the disease: (1) faucial diphtheria, (2) nasal diphtheria, (3) laryngeal diphtheria (croup), (4) ocular diphtheria, (5) vaginal diphtheria, and (6) cutaneous or surgical diphtheria.

The following forms are distinguished according to the degree of intoxication: (1) mild, (2) subtoxic and (3) toxic.

The general scheme of classification of the clinical forms of diphtheria is given below (Table 6).

The following are the main clinical varieties of the disease.

1. *Faucial diphtheria.* Faucial diphtheria may involve only the area of the tonsils—localized form (Fig. 76)—or also the palatine arches, soft palate and nasopharyngeal mucosa—diffuse form.

The *localized* form of faucial diphtheria is the most frequent. In

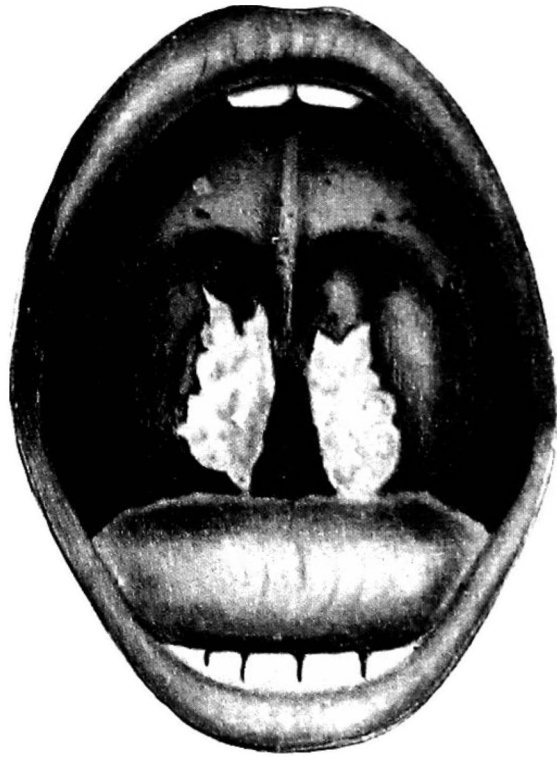


Fig. 76. Localized form of leucoplakia.

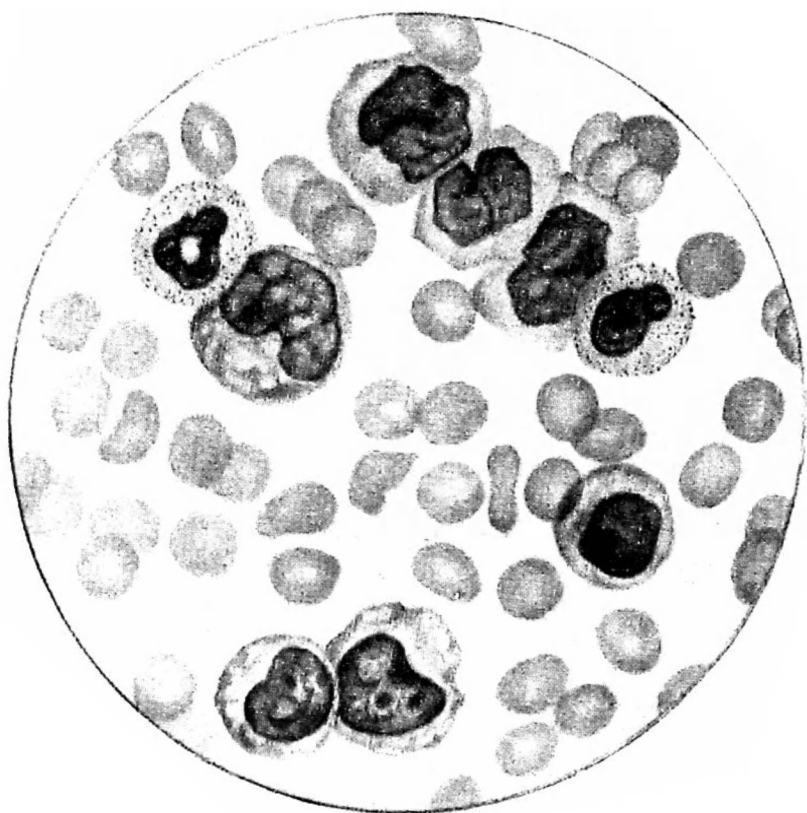


Fig. 82, Blood picture in infectious mononucleosis showing plasmacytes

cases of moderate severity the disease sets in with a moderate rise in temperature (up to $38.3-38.4^{\circ}\text{C}$), feeling of jadedness, sluggishness and slight pain on swallowing. Some 24-36 hours after the onset of the disease a mild hyperaemia of the fauces appears and small *insular* moderately dense whitish-grey membranes form on one or both tonsils; after these membranes are removed with a cotton swab or spatula the surface of the tonsils slightly bleeds.

The submaxillary and anterior cervical lymph nodes enlarge on the side of the affection (and in cases of affection of both tonsils – on both sides).

In such cases the disease runs a rather mild course and, if serum treatment is instituted in due time, the patient's condition becomes quite satisfactory within 2-4 days, the membranes on the tonsils disappear and the temperature returns to normal.

The diffuse form of the disease sets in acutely with chills and a rise in temperature to $38.5-39^{\circ}\text{C}$; the general intoxication of the organism is sometimes strongly pronounced.

Examination of the patient's fauces reveals considerable hyperaemia and oedema of the tonsils on which there are massive, dense membranes which are difficult to separate from the underlying tonsillar tissue. The membranes spread to the mucosa of the nasopharynx, palatine arches and soft palate. In toxic diphtheria the patient's mouth sometimes emits a peculiar sweetish odour which is the more pronounced, the more extensive the affection of the fauces. The submaxillary and cervical lymph nodes are, as a rule, enlarged and slightly painful on palpation; they do not adhere to each other or to the surrounding tissues.

Even with timely and vigorous serum treatment the membranes disappear from the fauces only between the 7th and 9th days of the disease.

The toxic and haemorrhagic forms of faucial diphtheria run a particularly severe course. In the former form the diphtheritic toxin severely affects the cardiovascular and nervous systems. From the end of the second week the disease is marked by tachycardia, arrhythmias, extension of the heart borders, extreme dullness of the sounds at all orifices of the heart and an unclear first sound; a gallop rhythm is possible, the liver may enlarge as a result of right ventricular insufficiency, and symptoms of toxic nephrosis may appear.

In some toxic diphtheria patients paresis of the soft palate may develop between the 10th and 12th days of the disease, and polyneuritis accompanied by paresis of the pharyngeal and laryngeal muscles—between the 22nd and 28th days. The cardiac changes are also recorded electrocardiographically (increase in the *P-Q* and *Q-T* intervals and flattening or inversion of the *T* wave). The early manifestations of the malignant syndrome in toxic faucial diphtheria are characterized by pallor of the skin, cyanosis of the mucosa of the lips, tachycardia, oedema of the cervical subcutaneous tissue,

Table 6

General Classification of Clinical Forms of Diphtheria

Form		Faucal diphtheria	Nasal diphtheria	Vaginal diphtheria	Ocular diphtheria	Laryngeal diphtheria
Mild	1. Localized	Catarrhal Membranous: (a) insular (b) continuous (membranes only on tonsils)	Catarrhal Membranous	Catarrhal Ulcerative Membranous (labia and vagina affected)	Catarrhal Membranous (only inner corns of lids affected)	Moderately severe form Laryngitis
Moderately severe	2. Diffuse	Membranes on tonsils, palatine arches, tongue, walls of pharynx and oral cavity	With affection of sinuses	With affection of perineum and anus	With affection of eyeball	Severe form (a) Laryngo- tracheitis (b) Laryngo- tracheo- bronchitis
	3. Combined	Affection of several nonadjacent systems (for example, ocular diphtheria and nasal diphtheria, etc.)				
	4. Toxic	Subtoxic: (a) oedematous (oedema of the fauces) (b) with unilateral cervical oedema Toxic: (a) without lymphatic enlargement;	Extensive membranes only in the nose with oedema of cervical subcutaneous tissue or simultaneously toxic faucial diphtheria	With oedema of the subcutaneous tissues of the vagina, pubes and thigh	With oedema around the eye	Simultaneously with toxic faucial diphtheria

Typical Forms

		(b) with haemorrhagic phenomena <i>First degree:</i> oedema of subcutaneous tissue up to second cervical fold <i>Second degree:</i> oedema up to clavicle <i>Third degree:</i> below the clavicle <i>Hypertoxic:</i> (a) fulminant without haemorrhagic phenomena (b) haemorrhagic	Nasal haemorrhages	Membranes impregnated with blood
Atypical	Severe			
	Without membranes, but with diphtheria bacilli at the site of the process	Crusts, erosions, granulations in the nose (subacute, relapsing, chronic rhinitis); paronychia, phlegmons, eczema, impetigo, umbilical diphtheria, intertrigo, long-unhealing wound, otic diphtheria		
	Without a visible local process, but with diphtheria bacilli in the nose and fauces	Dyspepsia, pneumonia in infancy with diphtheria bacilli present in the nose or fauces. Oesophageal and gastric diphtheria		
	Diphtheria mixed with other infections	In measles (croup), scarlet fever (angina and croup), whooping cough (croup), influenza (croup)		
	Forms of diphtheria according to the course of the disease	Acute, subacute, relapsing		

sweetish odour from the mouth, and physical and electrocardiographic symptoms of myocardial affection.

The severe haemorrhagic form is marked by a petechial eruption on the skin, nosebleed and the presence of blood-soaked membranes on the fauces. In many patients the blood picture is characterized by leucocytosis (15,000-20,000 leucocytes per 1m^3), thrombocytopenia and aneosinophilia; 25-30 per cent of the patients exhibit monocytosis. The capillaries become more fragile.

The catarrhal form of diphtheria is a special variety of the disease; it is characterized only by a catarrhal process—hyperaemia of the tonsils and presence of diphtheritic bacteria in smears taken from the fauces. Such cases are very difficult to diagnose. Patients with faucial catarrh and diphtheritic bacteria in smears taken from the fauces must be suspected of diphtheria and treated with antitoxic serum. The catarrhal form of faucial diphtheria usually runs a mild course, but it may also be accompanied by toxic myocarditis.

Nasal diphtheria most commonly occurs in infants. This variety of the disease may be observed in one of the two following forms—membranous and catarrhal. In the former the infant develops respiratory difficulties and a discharge from the nose—at first serous and then sanious and purulent. Rhinoscopy reveals membranes on the nasal septum and conchae.

In patients with the catarrhal form of nasal diphtheria haemorrhagic crusts and erosions form on the nasal mucosa.

In nasal diphtheria the organism is either moderately intoxicating or not at all, and the temperature may be subfebrile.

Laryngeal diphtheria (true croup) may be a separate disease entity or may be concurrent with faucial or nasal diphtheria in which cases the membranes spread to the laryngeal mucosa.

For practical purposes it is very important to diagnose true croup at the earliest stage of its development which lasts 1-3 days and is accompanied by a dry, barking cough and a husky voice which subsequently weakens to the point of aphonia. If no appropriate measures are taken, stenosis develops. Inhalation is rendered very difficult, and the most pliable parts of the chest sink. Finally the stage of asphyxia develops; it is characterized by marked oxygen deficiency (cyanosis of the nose, lips and finger tips, cold hands and feet). Further deterioration of the pulse and increasing arterial hypotension lead to the patient's death.

Diphtheritic croup may be caused directly by affection of the larynx with the presence of membranes in it (primary croup) or by transition of the pathologic process from the mucosa of the fauces or, as is less frequently the case, from the nasal mucosa (secondary croup).

The mildest form of diphtheritic croup is its *localized form*; serum treatment usually suffices to liquidate the morbid phenomena in this form of croup.

The diffuse form may involve the larynx and trachea (form A

croup or diphtheritic laryngotracheitis) and additionally the bronchial tree (form B diphtheritic croup or diphtheritic laryngotracheobronchitis).

As a rule, croup affects very young children and is second, after faucial diphtheria, in incidence among the other clinical varieties of diphtheria.

Extensive membranes in the larynx, trachea or bronchi may almost completely close the air passages and cause asphyxia. Disorders of external respiration (due to reflex spasm of the larynx and ensuing asphyxia) are possible even in cases where the fibrinous membranes forming on the mucosa of the larynx, trachea or bronchi do not directly hinder inhalations or exhalations.

Diphtheritic croup is not infrequently complicated by pneumonia which, like increasing asphyxia, serves as the cause of death in severe cases of the disease.

At the onset of diphtheritic croup the rise in temperature and increasing sluggishness of the child with feebly marked symptoms of general intoxication are followed by hoarseness and a dry, coarse cough. This first period of croup lasts 1-2 days after which the disease enters the stenotic period with development of aphonia (the patient's voice and cough become soundless); respiration is laboured and of a marked stenotic character. It is particularly characterized by a noisy passage of the air through the stenosed glottis. The most pliable parts of the chest (supraclavicular fossae, intercostal spaces) are drawn in during inhalation.

The stenotic state manifests itself in attacks recurring over a period of 2-3 days. During this period the treatment is limited to application of revulsants (hot foot baths), complete rest and fresh air, and administration of bromides.

Subsequently, as the attacks become more frequent and the intervals between them shorter, the third and most dangerous period of diphtheritic croup—asphyxial period—develops. The child becomes extremely restless, grows very pale, tosses about in great fright, his skin is covered with sticky sweat and his pulse is very fast. This dangerous state of oxygen deficiency may result in death unless a timely *intubation* or a *tracheotomy* is performed.

Intubation is the introduction of a metal tube by means of a special instrument (intubator) into the larynx to ensure the passage of air into the trachea. The intubation tube is introduced by a physician (or physician's assistant) with the aid of a nurse or medical attendant. Before performing the intubation it is necessary to prepare the entire set of requisite instruments and accessories (intubator, a set of tubes of different calibres in accordance with the patient's age, mouth retractor, spatula, silk thread to remove the tube, bandages, etc.).

An attendant wraps the child up in a sheet so that the child's arms and legs are immobilized and sits down with the child, while



Fig. 77. Intubation scheme

a nurse stands somewhat to the rear and to the left of the child and introduces a mouth retractor into the child's mouth with the aid of a spatula. The nurse must set the branches of the retractor on the left molars and must part the jaws as wide as possible.

The physician (or assistant) who performs the intubation sits down opposite the child and, holding the intubator with the intubation tube to which a silk thread is attached in his right hand, introduces his left forefinger into the child's mouth all the way to the epiglottis. Moving the epiglottis forward he presses it with the same finger to the root of the tongue.

Along the forefinger the physician (or assistant) introduces the intubator with his right hand into the pharyngeal cavity (Fig. 77) and then raises the intubator handle to introduce the intubation tube into the larynx.

The introduction of the intubation tube into the larynx is followed by a peculiar noise, made by air passing through the larynx into the respiratory tract, and a short dry cough; the patient's face and lips turn pink, the fright and anxiety disappear.

To fix the intubation tube in the larynx, the physician (or assistant) must hold it in place with the left forefinger and only then remove the intubator with the right hand. The thread fastened to the intubation tube is fixed on the patient's cheek with adhesive plaster. The sick child feels enormously relieved and usually falls asleep.

To prevent the child from removing the tube by pulling the thread, his arms are bandaged to his body or his hands are immobilized by splints.

The intubation tube is left for 2-3 days and is then removed for it may produce necrosis of the tissues (decubitus ulcers). In some cases of continued stenotic respiration the intubation must be repeated.

Intubated patients need careful watching by the medical personnel and frequent feeding with small portions of semiliquid, easily assimilable, high-calory, vitamin-rich food. At the same time these patients are given serum treatment (in diffuse forms A and B croup a single dose of serum must be 20,000-30,000 U, the total course dose—60,000-80,000 U).

In severe asphyxial cases of diphtheritic croup with obvious extensive membranes in the larynx and trachea (the membranes being partly discharged during coughing), as well as in cases where croup is combined with faucial diphtheria and in the descending form of croup (diphtheritic laryngotracheobronchitis) a *tracheotomy* must be resorted to. This is a bloody operation. A surgical incision is made in the skin on the anterior surface of the neck and in the subcutaneous tissue, and the muscles and fasciae are parted. The exposed trachea is cut with a scalpel over an area of 2-3 cartilaginous rings, and a tracheotomic tube is inserted in the orifice formed by the incision and is fastened to the neck with a gauze bandage. The bandage over the tube is moistened with a 1 per cent soda solution. An upper or lower tracheotomy is made, according to indications.

In some cases, when the intubation cannot be repeated, but the child cannot breathe without a tube, the *tracheotomy has to be repeated*; it should be remembered that this operation often leads to a cicatricial narrowing of the larynx and the tube must be left in the trachea for the rest of life.

Timely and vigorous treatment makes it possible to bring the diphtheritic croup patient out of his extremely grave condition.

Ocular diphtheria is a relatively rare clinical form of diphtheria. It may manifest itself as a croupous or membranous affection of the eyes.

In the former case severe oedema of the eyelids develops so that the palpebral fissures are either considerably narrowed or closed. Thin greyish-white membranes are visible on the conjunctiva of the lids, and the eyes discharge a purulent or pyosanguineous substance.

In the membranous form of ocular diphtheria a massive, dense oedema of the lids develops with massive dirty-grey or dirty-yellow membranes on their conjunctivae; a seropurulent and later a purulent discharge are often observed. The croupous form must be bacteriologically differentiated from conjunctivitides caused by pneumococci, and the membranous form—from conjunctivitides caused by the Coxsackie virus (simultaneous attack of several persons).

Complications. Complications more often accompany severe forms of diphtheria than moderately severe or mild forms. However, various complications, especially in the cardiovascular system, may also occur in the latter forms.

Early paralysis of the heart (on the 3rd or 4th day of the disease) is possible in toxic forms of diphtheria.

Between the 8th and 15th days of the disease diphtheria may be



Fig. 78. How a child must be held for taking a specimen of mucus from the fauces to be tested for diphtheritic bacteria

accompanied by development of severe myocarditis; clinically this complication is characterised by extreme pallor of the patient, tachycardia, extension of the percussion borders of the heart, extreme dullness of the heart sounds, systolic murmur, fall of the blood pressure, and a soft pulse easily compressible by palpation. The liver is enlarged, and the urine contains protein. Diphtheritic myocarditis may lead to progressive circulatory insufficiency and even death. But with bed rest and appropriate treatment the symptoms of myocarditis gradually disappear.

Peripheral paralyses sometimes develop between the 15th and 22nd days of the disease; accommodation paralysis and paralysis of the soft palate (the patient's voice acquires a nasal twang, the soft palate sags, and upon attempts to swallow water the latter comes out through the nose) are particularly characteristic.

Paralyses of the laryngeal and pharyngeal muscles and sometimes of the lower extremities are possible, especially in small children; pneumoniae and polyneuritides may develop.

An attack of diphtheria confers a certain degree of immunity, but the disease may recur.

Diagnosis. Diphtheria is diagnosed on the basis of a careful analysis of the clinical and epidemiological data; a confirmation of the diagnosis by finding diphtheritic bacteria in smears of mucus taken from the fauces and nose (Figs. 78 and 79) is desirable.

For a bacteriologic examination a smear is taken separately from the fauces and nose with a cotton tampon soaked in horse serum for subsequent inoculation in a coagulated blood serum. The laboratory produces results within 24-36 hours. It should be emphasized that even in the absence of a laboratory confirmation of diphtheria it is necessary to administer treatment with antitoxic serum in all cases where this disease has been diagnosed on the basis of the clinical picture.

For retrospective diagnosis of doubtful cases a dynamic agglutination test may be performed from about the 5th or 7th day of the disease.

Differential diagnosis. The disease must be differentiated from Vincent's angina, catarrhal, follicular and lacunar anginas, and the anginous-bubonic form of tularaemia.

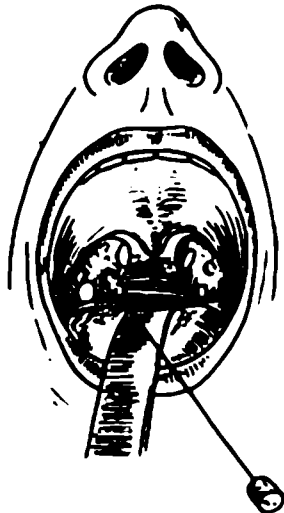
Vincent's angina is characterized by formation of an ulcer on one of the tonsils; the floor of this ulcer is covered with a loose dirty-yellow film; the affected tonsil is hyperaemic, the regional lymph nodes (submaxillary) are enlarged and slightly painful, but there is no oedema of the cervical subcutaneous tissue; a peculiar putrid odour is emitted from the mouth. The patient's temperature rises to 39-39.5 C.

Catarrhal and follicular anginas are characterized by a much higher temperature than diphtheria.

Follicular angina is accompanied by extreme hyperaemia of the tonsils and formation of films which look like rather large yellowish islets on the tonsils; swallowing is painful.

In lacunar angina the temperature also rises considerably, and there are easily removable films in the crypts of the tonsils.

Phlegmonous angina is accompanied by a high temperature.



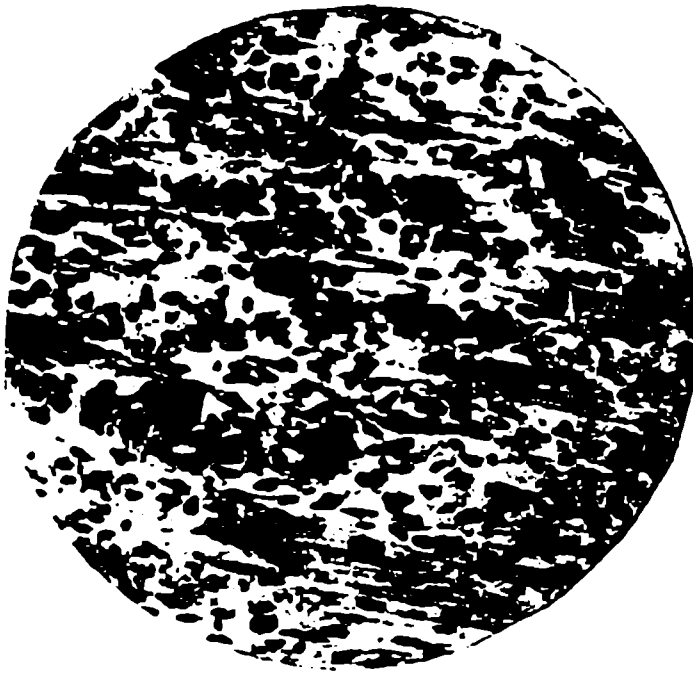


Fig. 80. Parenchymatous myocarditis in toxic diphtheria
(from A. I. Abrikosov and A. I. Strukov)

oedema and extreme hyperaemia of the affected tonsil; swallowing is very painful.

Tularaemic angina exhibits a necrotic film on one of the tonsils and enlarged submaxillary and anterior cervical lymph nodes.

Preliminary results of an examination for diphtheritic bacteria may be obtained by microscopy of a Neisser-stained smear taken from the patient's fauces or nose. An auxiliary role in the diagnosis of diphtheria is played by a tellurite test; the diphtheritic membranes swabbed with a 2 per cent sodium tellurite solution turn black. An agglutination test of a special killed culture with the patient's blood serum was recently proposed for the diagnosis of diphtheria (a demonstrative titre of 1:200 or higher is obtained on the 5th or 6th day of the disease).

In establishing a differential diagnosis of croup it should be remembered that false croup usually appears at night and develops suddenly without aphonia.

Prognosis. In diphtheria the prognosis is determined by the severity of the disease, the time serum treatment is instituted, and the development of complications, especially in the myocardium (Fig. 80)

and the peripheral nervous system (polyneuritides). It should be remembered that these complications may develop 10-15 days after abatement of the acute manifestations of the disease.

Treatment. All diphtheria patients must be hospitalized. Severe cases need thorough care.

Diphtheria patients must be prescribed a diet of semiliquid, easily assimilable, high-calory food. It is necessary to saturate the organism with vitamins C and B. The daily ascorbic acid requirement for older children and adults affected with diphtheria is 300-500 mg. Children 8-9 years old must be given 0.008 g of vitamin B₁ (thiamine) per os 3 times per day for 10 days.

Bed rest is required for 9-12 days in mild forms of diphtheria, and for 4-5 weeks in subtoxic and toxic forms.

Cardiovascular activity must be supported by intravenous infusions of glucose and subcutaneous injections of ephedrine, cordiamine, strychnine and camphor; these agents are particularly necessary in cases of development of myocarditis; they are administered according to indications.

Development of peripheral paralyses requires intramuscular administration of vitamin B₁ (1 ml of a 0.5 per cent thiamine bromide solution for adults) and proserine (neostigmine) (1 ml of a 0.05 per cent solution per day for adults).

In cases of diphtheritic croup, vapour inhalations of atomized soda, and codeine per os (to mitigate the cough) must be administered. In cases of increasing stenosis and laboured respiration it is necessary to perform an intubation; sometimes, however (for example, in descending croup), intubation may not eliminate stenosis and asphyxia. In such cases it is necessary to resort to a tracheotomy.

The principal agent in the treatment of diphtheria is an antidiphtheritic serum produced by immunization of horses with diphtheria toxin or anatoxin.

To diminish the possible serum sickness phenomena (see p. 75), "diaferm" serums cleansed of the ballast proteins by fermentation are used.

The first time the serum is administered by the method described on page 75 or by the much simpler Besredka's method described on the same page, to prevent the anaphylactic shock which sometimes occurs when serum is administered.

The dose of serum to be given is determined by the concrete clinical form, severity and duration of the disease. The serum is administered repeatedly over a period of several days in accordance with the patient's general condition and the character of local affections (see Table 7).

On the first day of treatment patients affected with the diffuse form of diphtheria are given 15,000-20,000 U, patients with the toxic form—25,000-60,000 U.

In the event of faucial necroses, simultaneously with antitoxic

Table 7**Average Serum Doses (in U) for Different Forms of Diphtheria**

Form of diphtheria	First single dose	Average dose per course of treatment
Localized form of faucial diphtheria	5,000-10,000	5,000-20,000
Diffuse form of faucial diphtheria	15,000-20,000	30,000-40,000
Subtoxic form of faucial diphtheria	20,000-30,000	40,000-50,000
Toxic form of first degree faucial diphtheria	20,000-30,000	40,000-60,000
Toxic form of second degree faucial diphtheria	30,000-40,000	60,000-100,000
Toxic form of third degree faucial diphtheria	40,000-50,000	120,000-200,000
Hypertoxic and haemorrhagic diphtheria	50,000-60,000	120,000-250,000
Nasal diphtheria (except the toxic form)	5,000-10,000	5,000-20,000
Laryngeal diphtheria	10,000-20,000	10,000-40,000
Laryngeal diphtheria in the second and third stages	20,000-30,000	40,000-60,000
Descending diphtheritic croup	30,000-40,000	60,000-80,000
Genital and ocular diphtheria	10,000-15,000	15,000-30,000
Cutaneous diphtheria	10,000	10,000-30,000

antidiphtheritic serum the patients are administered penicillin to prevent secondary infection.

In cases of diphtheritic croup the question of whether intubation or a tracheotomy is necessary is decided while the patients are treated with antitoxic serum.

Children affected with diphtheritic paralyses involving disorders of deglutition are fed artificially by means of a thin feeding tube through the nose (see Fig. 10); the slightly-heated nutrient mixture consists of 50 g of sugar, 50 g of butter, 1 egg, 200 mg of vitamin C and 150 g of milk. In view of the danger of asphyxia developing in such children 2 nurses must be present at the artificial feeding ready to administer aid in case of emergency.

Prevention. Every diphtheria patient is subject to hospitalization (contagious department) regardless of the clinical form of the disease.

The apartment or hostel where the patient lived before hospitalization must be thoroughly disinfected (moist or formalin disinfection). Persons who were in contact with patients are subject to quarantine until negative results of the bacteriological examination of mucus taken from the fauces and nose are obtained; this applies to children, as well as to adults working at medical and children's institutions and food-handling establishments. If a bacteriological examination is impossible, the quarantine ends 7 days after isolation of the patient.

An important role in controlling the infection is played by revelation of bacteria carriers who must be kept out of children's institutions (nurseries, kindergartens, young pioneers' camps). It should be emphasized that bacteria carriers can be revealed only after a number of smears of mucus are taken from the fauces and nose and are examined for Loeffler's bacilli; discharge from the hospital is allowed after two examinations of mucus from the fauces and nose with negative results.

No radical methods of liquidating bacteria-carrying have been elaborated. Sometimes inoculation of the material taken from the fauces or nose temporarily ceases to yield diphtheritic bacteria in cases treated with biomyacin (administered per os in doses of 200,000 U 4 times per day for 5-6 days for adults).

Inoculations with diphtheritic anatoxin serve as the method of specific prevention of diphtheria. All children 1-12 years of age should be vaccinated and revaccinated (according to special instructions). Children must be vaccinated at the age of 1-1.5 years; 1 ml (or 25 U) of diphtheria anatoxin is administered subcutaneously for the first inoculation. The second inoculation with 2 ml of the anatoxin is administered subcutaneously 20-30 days later. The first revaccination is performed by a single administration of 1 ml of anatoxin 3-6 months after the vaccination. Children must be revaccinated at 3-4, 7-8 and 12 years of age.

Schemes for inoculations with an adsorbed diphtheria anatoxin and a pertussis-diphtheria-tetanus vaccine have now been elaborated.

INFECTIOUS MONONUCLEOSIS

Actiology. The disease is caused by a filtrable virus — *Glandulophyllus infectiosa*.

Epidemiology. The role of the source of infection is played by patients and virus carriers; it is an air-borne infection and may occur in single cases and in rather extensive epidemics. It is most commonly observed during autumn and winter months.

Clinical picture. The incubation period is about 7-12 days. The disease sets in acutely, with chills and a rapid rise in temperature. Soon pain on swallowing appears; examination of the fauces reveals catarrhal, ulcerative or lacunar angina with dirty-grey necrotic films on both tonsils during the first days of the disease. Then the submaxillary, anterior cervical and, especially, posterior cervical lymph nodes become enlarged (Fig. 81). Often other groups of lymph nodes—axillary and inguinal—are enlarged and polyadenitis develops. In many cases the spleen also enlarges.

The changes in the blood picture are characteristic; from the very first days of the disease leucocytosis moderately increases and the blood shows an increase in the number of lymphomonocytes. Between the 6th and 8th days of the disease the number of leucocytes increases to 12,000-18,000 per 1 cu mm of blood, and lymphomonocytosis and plasmacytes are observed (Fig. 82). The febrile period lasts 20-25 days, sometimes a little longer. As a rule, the disease ends in complete recovery; prolonged subfebrility and relapses of the disease are only rarely observed. Lymphomonocytosis persists for a long time.



Fig. 81. Infectious mononucleosis: enlargement of right cervical lymph nodes

Diagnosis. The disease is diagnosed on the basis of the clinical picture showing angina, polyadenitis and characteristic changes in the peripheral blood; in some cases the diagnosis is facilitated by epidemiological data—contact with an infectious mononucleosis patient. To confirm the diagnosis the Paul-Bunnell test is used; this test may be performed from the 4th or 6th day of the disease; the diagnostic titre is 1:64; if this test is performed later, the titre increases.

Differential diagnosis. The disease must be differentiated from faucial diphtheria, the anginous-bubonic form of tularemia, lymphocytic leukaemia and typhoid fever.

Treatment. All patients are hospitalized. There are no specific agents to treat this disease, but sometimes patients are relieved by penicillin (300,000 U intramuscularly 3 times per day for 6 days); in addition to penicillin it is advisable to give the patient medium doses of prednisone or prednisolone.

Prevention. The measures of preventing the spread of infectious mononucleosis are early isolation and treatment of patients in hospitals.

WHOOPING COUGH (PERTUSSIS)

Whooping cough is an extremely contagious disease affecting predominantly children; during the initial period it is characterized by upper respiratory catarrh which is followed by a protracted stage of coughing paroxysms.

Brief historical information. As a separate disease entity whooping cough was first recognized by clinicians in 1724.

The main ideas concerning the epidemiology and clinical aspects of whooping cough formed in the 19th century. The studies of the Russian scientist M. I. Afanasyov, dating from 1887-1907, and of the French microbiologists Bordet and Gengou, carried out in 1906-1907, established the aetiology of the disease (Bordet-Gengou bacillus) and clarified a number of questions of whooping cough immunology.

In 1950 synthomycin and levomycetin were successfully used in the treatment of whooping cough, thereby laying down the foundation of chemotherapy of this disease. Biomycin and tetracycline began to be used later. Methods of vaccination have been elaborated.

Aetiology. The disease is caused by the Bordet-Gengou bacillus (*Hemophilus pertussis*)—gram-negative, nonmotile rod with rounded ends. The Bordet-Gengou bacillus stains very well (its ends staining particularly intensively) with aniline dyes. A pure culture of the causative agent of whooping cough is produced on glycerin-potato blood agar.

Cold does not diminish the viability of the bacillus; heating to 56° C kills it.

Epidemiology. Whooping cough is observed mainly in children 2-4 years of age. Younger and older children are affected much less frequently. Now and then the disease attacks adults.

Patients mainly in the first, catarrhal, stage of whooping cough are the source of infection in all cases.

Whooping cough is an air-borne infection and is transmitted through rather close contact with patients.

Pathogenesis and pathologic anatomy. Transmitted through the air (in droplets) to the upper respiratory mucosa the Bordet-Gengou bacilli spread along the trachea and the bronchial tree and produce

inflammatory changes in the mucosa; the changes are most clearly manifested in the arytenoid area and in the bifurcation of the trachea. A catarrhal process clinically manifesting itself in diffuse bronchitis develops on the upper respiratory mucosa. The endobronchitis is followed by peribronchitic processes, and the lymph circulation in the pulmonary tissue is disorganized. Later, as the whooping cough bacilli multiply and, as a result of their destruction, liberate an exotoxin, the mucosa of the respiratory tract becomes sensitized and the sensory nerve endings are continuously irritated by the toxic products with resultant paroxysms of coughing of reflex and allergic character.

An important role in the coughing paroxysms of whooping cough is played by the direct action of the exotoxin on the central nervous system. The participation of the central nervous system in the pathogenesis of coughing paroxysms is obvious from the well-known clinical fact that by transferring the sick child's attention to other objects or phenomena, for example, by showing him an interesting toy or by clapping the hands, it is possible to arrest the paroxysm.

The signs of oxygen deficiency (cyanosis, dyspnoea) observed during severe coughing paroxysms are due to the action of the exotoxin on the respiratory centre. Postmortem examination of patients who have died of whooping cough reveals pulmonary emphysema and inflammatory changes in the mucosa of the trachea and bronchi.

Bacteriological tests of the sputum of whooping cough patients show Bordet-Gengou bacilli.

An attack of the disease confers lifelong immunity.

Clinical picture. The incubation period of whooping cough is 2-21 days. The first clinical symptoms of the disease are general indisposition, husky voice, mild rhinitis and cough with hyperaemia of the posterior laryngeal wall—*catarrhal* period of whooping cough. Sometimes this period is accompanied by a slight rise in temperature. During the 4-5 days immediately following the catarrhal phenomena in the upper respiratory tract increase and numerous dry rales are auscultated in the lungs. The considerable resemblance of the clinical picture of whooping cough of this period to ordinary diffuse bronchitis renders early diagnosis of the disease extraordinarily difficult; yet it is during this period that the patients are particularly contagious. The catarrhal period lasts 8-10 days, sometimes a little longer. Then the disease enters the most characteristic stage—the *paroxysmal* stage.

At the onset of the paroxysm the sick child's respiration is suppressed and several convulsive coughs occur; the coughs are accompanied by a burning and tickling in the larynx and trachea, and after a brief pause are followed by a deep inhalation and a paroxysm of coughing during which the patient's face puffs up, turns red and cyanotic. As a result of an increased exhalation the tongue is thrust out and somewhat curved upward. If the paroxysms are frequent, a

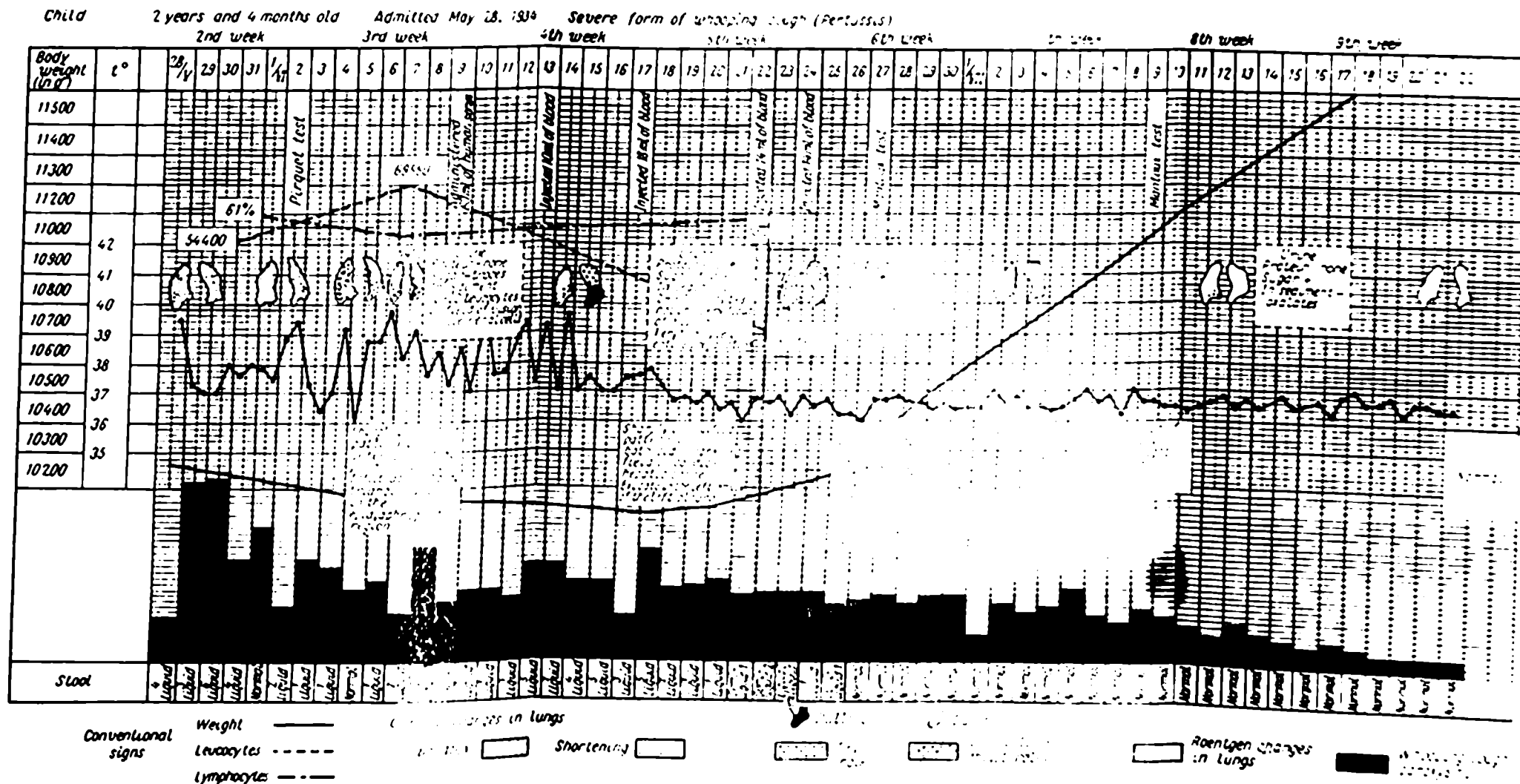


Fig. 83. Severe form of whooping cough in child 2 years and 4 months old not treated with antibiotics

small ulcer forms on the frenulum of the tongue (injury of the frenulum by the teeth), and nosebleed and haemorrhages into the conjunctivae are possible. In many children the paroxysms of coughing are accompanied by vomiting, in some cases—by involuntary urination and defaecation.

Several successive convulsive coughs are followed by a long whooping sound due to the passage of air through the theretofore closed glottis. The convulsive coughs are accompanied by contraction of all the respiratory muscles. At the end of each paroxysm a small amount of viscous glasslike mucus is discharged.

A very few minutes after the end of the paroxysm the sick child's condition becomes so satisfactory that the child can play and skip about merrily.

Subsequently, however, for 2-3 weeks of the paroxysmal stage of the disease, the paroxysms occur more frequently and are longer and more severe; in the course of a day the child may have from 8-10 to 30-40 paroxysms. The paroxysmal stage of whooping cough lasts 3-4 weeks, then the paroxysms occur less frequently and become shorter and less distressing; this is the stage of resolution of the disease. The sputum discharged by patients at this period is very heavy and greenish. By the 5th or 6th week of the disease the paroxysms cease and the discharge of sputum ends. Blood tests during the paroxysmal stage of the disease (and sometimes even earlier) reveal leucocytosis (12,000-50,000 leucocytes per 1 cu mm), lymphocytosis and a slower ESR. The specific gravity of the urine is increased. Uncomplicated whooping cough lasts from 1.5 to 2.5 months.

Complications. Whooping cough is accompanied by frequent and distressing paroxysms of coughing which cause forced exhalations and lead to development of acute pulmonary emphysema. An addition of a secondary infection whose causative agents live on the mucous membranes of the upper respiratory tract, and the action of the whooping cough bacteria (*Hemophilus pertussis*) may give rise to micro-focal pneumoniae, peribronchitides and bronchiolitides with the result that the clinical course of the disease may become much more severe (Fig. 83). The symptoms of pertussal pneumonia are dyspnoea, cyanosis of the lips, shortening of the percussion sound in the lower lobes of the lungs and the presence of moist vesicular rales in them. An attack of the disease confers lifelong immunity.

Diagnosis. In the absence of direct epidemiological indications whooping cough is extraordinarily difficult to diagnose during the catarrhal period, especially in single (sporadic) cases. The diagnostic problem is greatly facilitated if the physician knows that the child has had close contact with a whooping cough patient or a case of whooping cough has been discovered in the institution (nursery, kindergarten, school) the child attended during the preceding 3-4 weeks.

Whooping cough is very easy to diagnose when paroxysms of

coughing appear. Cultivation of whooping cough bacilli in Petri dishes containing a special agar (cough plates) and an allergic skin test are used for laboratory diagnosis.

Prognosis. Whooping cough runs the severest course in infants; with age the prognosis becomes more favourable. A severe course of the disease and development of complications (especially pneumoniae and bronchiolitides) render the prognosis very serious, if no antibiotics are used. The prognosis is also aggravated when whooping cough is combined with measles, pulmonary tuberculosis or dysentery.

In older children the prognosis is usually favourable if the disease does not run a severe course.

Treatment. Whooping cough patients are usually isolated at home. Serious cases, especially cases of mixed infection or those involving complications, should be hospitalized.

The room or ward of whooping cough patients must be well ventilated or more frequently aired. Whooping cough patients must walk and sleep outdoors as often as possible.

If whooping cough has broken out in a children's institution, it is necessary to separate a special "whooping cough group" and give the affected children health resort treatment.

Children affected with whooping cough must be given palatable, easily assimilable and sufficiently caloric food enriched with vitamins, especially vitamin C. Infants in the first months of life must be fed the breast.

Patients in the catarrhal period of whooping cough are advised to drink warm alkaline mineral water and inhale the vapours of a heated 2 per cent soda solution. In cases accompanied by severe attacks of asphyxia the patients must be given enemas of a 2 per cent chloral hydrate solution in starch water.

The doses must correspond to the child's age: from 6 months to 3 years of age—0.15 g of chloral hydrate, 3-4 years of age—0.2 g, 4-7 years of age—0.25 g, and 7-12 years of age—0.4 g.

Favourable results, especially in the early stages of whooping cough, are observed after a 6-7-day course of levomycetin treatment; the antibiotic is administered in single doses of 0.02 g per 1 kg of the child's weight. Adults are given levomycetin in a dose of 0.5 g six times per day for 6-7 days. Good results are also produced by treatment with biomycin in a dose of 0.025 g per 1 kg of the child's weight per day; tetracycline is administered in the same doses.

Prevention. The most important role in preventing whooping cough is played by early revelation of patients, their isolation from healthy children, and organization of 3 groups in nurseries and kindergartens: (a) patients, (b) children affected with bronchitides, and (c) healthy children (quarantined for 30 days from the appearance of a paroxysm of coughing in the first child of the given group).

All healthy children who were in close contact with a whooping cough patient must be subjected to passive immunization against whooping cough by intramuscular administration of normal human serum (45-60 ml) or gamma-globulin. This method is not very effective, however.

Soviet investigators have now elaborated methods of active immunization against whooping cough by inoculations with special vaccines. The whooping cough vaccination may be combined with diphtheritic anatoxin.

Children who have had an attack of whooping cough may not be admitted to children's institutions before at least 30 days have elapsed since the appearance of paroxysms of coughing because only by that time do they cease to be contagious.

Staying outdoors (in specialized children's sanatoriums and forest schools) for 24 hours a day fosters the quickest possible recovery of whooping cough patients and thereby the termination of their contagiousness. In winter such children must sleep in special sleeping bags on verandas and balconies.

MEASLES (MORBILLI)

Measles is an extremely contagious disease, mainly of children. It is characterized by eruptions on the skin, enanthema, upper respiratory catarrh and conjunctivitis.

Brief historical information. The disease was known already in antiquity, but was given a full-enough scientific description only by Panum who observed it on Faroe Islands where an epidemic of this disease in 1846 affected nearly 75 per cent of the population. A brilliant description of the clinical aspects of measles was given in the lectures and monographs of N. F. Filatov. The early diagnostic sign of the disease—branny desquamation of the oral mucosa—was described by A. P. Belsky, a Pskov physician, in 1890 and by N. F. Filatov in 1895. An analogous sign was described later (in 1896) by G. Koplik. The works of Degkwitz on measles prevention by injection of the blood serum of adults to children who have had contact with measles patients were published in 1921. The causative agent of the disease has been produced in cultures. The possibility of producing an effective vaccine is being investigated.

Aetiology. The causative agent of measles is a special type of virus—*Polynosa morbillorum*. In the external environment the virus is quickly destroyed, but immediately after its discharge in particles of mucus from a patient's upper respiratory tract it may be carried by the air current over considerable distances—from one room to another, through corridors, etc.—which accounts for the high contagiousness of measles patients. The sources of infection are patients from the last 2 days of incubation to the 4th day of the eruption and but rarely during later periods. It is necessary to emphasize the epidemiological importance of patients affected with atypical or effaced forms of measles.

Epidemiology. The infection is transmitted to healthy susceptible humans through the air on rather close contact with patients. The

particles of mucus discharged from the respiratory tract and nasopharynx of patients during coughing or sneezing may come in contact with the mucosa of the respiratory tract of healthy susceptible people.

The movement of the measles virus with air currents makes possible the infection of people not only in the same room, but also in adjacent rooms.

Measles most commonly affects children up to 4 years of age; it may also attack adults who have never had the disease before.

An attack of measles confers lifelong immunity.

In areas where measles has never occurred before all of the population is susceptible and mortality is very high, as was the case on Faroe Islands in 1846, 1862 and 1875.

Pathogenesis and pathologic anatomy. On coming in contact with the mucosa of the upper respiratory tract the filtrable virus affects its epithelium. An acute catarrh develops and successively spreads to the bronchi, the bronchioles and around the bronchi where it gives rise to peribronchitis. In more severe cases of measles necroses of the mucosa of the upper respiratory tract are possible. Cases of primary morbillous pneumoniae which considerably aggravate the prognosis are not infrequent. The affection of the epithelium of the upper respiratory tract is soon followed by generalized infection (virusaemia). The foregoing main features of measles pathogenesis have been established by experimental production of the disease in monkeys.

In addition to phenomena of peribronchitis and focal pneumoniae postmortem examination reveals formation of abscesses in small foci of the lungs. Death is the result not of measles, but of concurrent complications. Some patients may, in addition to specific morbillous changes in the lungs, have necrotic processes due to streptococcal infection activated as a result of lowered general resistance. Measles often activates latent pulmonary tuberculosis or fosters increased susceptibility to it. Postmortem examination of people who have died of measles may therefore reveal a pathoanatomical picture of tuberculosis in an active stage.

Administration of antibiotics suppresses secondary infection.

Clinical picture. The incubation period averages 10 days, but in patients prophylactically given injections of antimeasles serum or gamma-globulin the incubation may last up to 28 days.

The incubation period is followed by a prodromal or *catarrhal* period of the disease. The temperature rapidly rises to 38.3-38.7°C, and the patients develop rhinitis, conjunctivitis, photophobia (Fig. 84) and a dry barking cough.

From the 2nd or 3rd day of the catarrhal (prodromal) period it is possible to observe on the mucosa of the patient's cheeks whitish areas of elevated branny desquamating epithelium—Belsky-Filatov-Koplik's sign. This sign plays a very important part

in the early diagnosis of measles because it makes it possible to reveal and isolate patients, and to administer antimeasles serum and gamma-globulin to all children who have had any contact with patients, all in good time. From the third day of the catarrhal period the hard palate exhibits diffuse hyperaemia. On the 4th day the temperature rapidly rises to 39.5-40.5°C; from this moment the *febrile* period or the period of eruptions begins.

A macromacular eruption, often of a confluent and papular character, appears on the skin of the face and behind the ears on the very first day of the febrile period; in between the lesions of the eruption the skin retains its usual appearance. On the 2nd day of the febrile period an eruption breaks out on the skin of the trunk and proximal parts of the extremities; on the 3rd day the eruption may also be seen all over the extremities. The eruption often consists of elevated round macules 3-4 mm in diameter with the separate macules tending to run together. Thus measles is characterized by a maculopapular eruption on the skin. In some patients, especially in extremely debilitated, emaciated children, the eruption may become cyanotic.



In uncomplicated measles the temperature falls to subfebrile or even normal figures by the 4th day of the eruption. The eruption disappears from the skin in the same sequence in which it appears (first from the face, then from the trunk and the extremities). The disappearance of the eruption is followed by a pigmentation and fine branny desquamation of the skin. During the febrile period the blood shows leucopenia with relative lymphopenia.

There are also severe forms of uncomplicated measles accompanied by a high temperature (up to 40°C), delirium, convulsions, dyspnoea and cyanosis; such patients are found to have phenomena of diffuse bronchiolitis. In such severe cases death may ensue even on the 2nd or 3rd day of the febrile period of the disease.

In adults measles runs a severe course, especially with concurrent disturbances in the cardiovascular system. Complications of the disease, primarily pneumoniae which may lead to paralysis of the respiratory and vasomotor centres, are the direct cause of death in measles, particularly in cases of children.

Mitigated (modified) *measles* is observed in children immunized with the blood serum of healthy people or with gamma-globulin. In these patients the temperature does not rise above 38°C, the eruption is scant and the disease does not last more than 4 days.

An attack of measles confers lasting immunity; reinfection is exceptionally rare.

Complications. The most frequent complications of measles are pneumonia and peribronchitis (high temperature, tachycardia, dyspnoea, shortened percussion sound in the postero-inferior parts of the lungs, bronchial respiration and moist microvesicular rales). In cases of measles complicated by pneumonia the temperature curve is essentially altered (Fig. 85). Complication of measles by pneumonia considerably aggravates the prognosis in all cases and requires vigorous therapeutic measures. In infants the disease may become complicated by capillary bronchiolitis which is accompanied by severe respiratory disorders (dyspnoea, cyanosis).

In some patients measles may become complicated by *false* (morbilious) *croup* which develops as an attack of asphyxia (usually at night) and is accompanied by oedema of the vocal folds. Morbillous croup develops during the catarrhal period or simultaneously with the outbreak of the eruption and is characterized by a barking cough, noisy respiration and a drawing-in of the pliable parts of the chest.

If a measles patient has developed false croup, no intubation is resorted to, but it is necessary most vigorously to use revulsive agents (hot foot baths with mustard) and oxygen inhalation.

In establishing a differential diagnosis in cases of croup it must be remembered that diphtheritic croup develops gradually; soon after the appearance of the initial symptoms of croup the voice is lost (aphonia); in morbillous croup phenomena of stenotic respiration

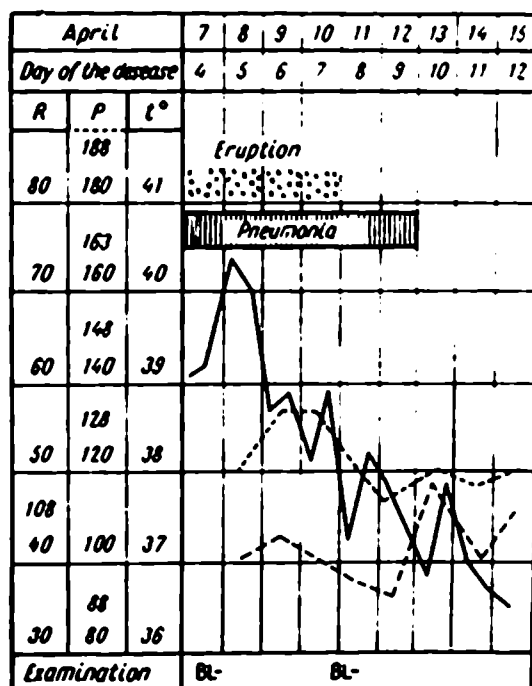


Fig. 85. Temperature curve in measles complicated with pneumonia (from M. G. Danilevich)

develop later, usually in 1-3 days, and lead to asphyxia if no requisite therapeutic measures are taken.

Measles may become complicated by *enteritis* with a frequent liquid stool and sometimes with vomiting. Addition of bacterial dysentery (tenesmus, frequent liquid stool with mucus and blood) aggravates the patient's condition. In some children affected with measles the development of colitis is apparently due to the changes produced by the causative agent of measles.

In younger children the complications of measles may be suppurative otitis, mastoiditis and sinusitides (highmoritis, ethmoiditis, frontitis).

Prognosis. In measles the prognosis is serious for children up to 3 years of age, especially in severe cases accompanied by complications extensively affecting the respiratory system (focal pneumoniae, peribronchitides). Measles runs a particularly severe course in debilitated and undernourished children.

The causes of death in measles are, as was already mentioned, complications (most commonly pneumoniae) and increasing cardiovascular insufficiency.

Diagnosis. During the catarrhal period and in the first 1-2 days of the eruption the diagnosis of measles is based on epidemiological anamnesis and the clinical picture of the disease with Belsky-Fi-

latov-Koplik's sign which is observed in 80-85 per cent of all measles patients (branny desquamation of the epithelium of the oral mucosa seen on the mucosa of the cheeks opposite the molars). The finding of this sign in a sick child makes it possible to carry out the necessary anti-epidemic measures in good time. The presence of catarrhal phenomena, the characteristic sequence of the skin eruptions and the blood picture help to establish the diagnosis at later periods of the disease.

Differential diagnosis. The disease must be differentiated from *rubeola morbiollosa*, typhus and various drug and serum eruptions associated, for example, with treatment with sulpha drugs or synthomycin. In *rubeola morbiollosa* the symptoms of the catarrhal period are less clearly marked, the eruption is finer than in measles, is polymorphous and localized mainly on the back and the extensor surfaces of the arms. Moreover, *rubeola morbiollosa* is characterized by enlargement of the occipital and posterior cervical lymph nodes.

The first 4-6 days of typhus are marked by persistent headache, puffy face, injected sclerae and conjunctivae (but not conjunctivitis!), petechial haemorrhages on the retrotarsal fold of conjunctivae, and polymorphous roseolous or roseolous-petechial eruption appearing on the 4th or 5th day of the disease and localizing mainly on the extensor surface of the arms, the lateral surfaces of the chest and on the back. It should be noted that the symptoms of the catarrhal period of the disease so characteristic of measles are absent in typhus.

In addition to their characteristic maculopapular appearance with a tendency to confluence of the various lesions, which is also typical of measles eruptions, drug eruptions are identified by a consideration of anamnestic data—the use of a drug which could have caused the eruption.

In addition to the appearance of papular and macromacular eruptions the serum sickness is often accompanied by a swelling of the joints.

Treatment and care. All measles patients must be isolated even if only at home; they must be kept in sufficiently light, warm and well-ventilated rooms, and must be given easily assimilable and highly caloric food with plenty of vitamin C and a lot to drink.

Because of conjunctivitis the patients' eyes must be washed with a 2 per cent boric acid solution at least twice a day. The patients must often gargle the mouth; in severe cases the mouth must be swabbed with a tampon soaked in a 2 per cent boric acid solution.

In cases complicated by pneumonia the patients must be administered penicillin injections, mustard plasters and mustard wrappings, intravenous infusions of physiologic solution and glucose, and cardiovascular preparations (cordiamine, caffeine). It is ad-

visible to combine penicillin treatment of pneumonia with administration of norsulphazol (sulphathiazole), and to give the patients plenty to drink. Penicillin may also be prescribed in the very beginning of the disease to prevent pneumoniae and purulent complications of measles.

In protracted cases of morbillous pneumonia haemotherapy is used—intramuscularly 10 ml of a healthy adult's blood and transfusions of small amounts (50-75 ml) of blood. To prevent hypostases in the lungs, patients must be turned over in bed more often.

Prevention. As soon as a measles patient is discovered he is isolated at home and all children from 3 months to 4 years of age who have been in contact with the patient are given an intramuscular injection of 30-60 ml of antimeasles serum or gamma-globulin, the dose depending on the physical condition of the children and the time of their contact with the measles patient. The question of inoculating children past 4 years of age is decided on the basis of medical indications. Inoculations must be administered to debilitated children and children who have recovered from other infectious diseases, for example, whooping cough, if they have had any contact with measles patients.

In admitting children to children's institutions (nurseries, kindergartens, hospitals, schools, young pioneers' camps) it is necessary carefully to reveal the epidemiological anamnesis and bar patients and children suspected of having measles from normal children's groups. Upon discovery of Belsky-Filatov-Koplik's sign or any other characteristic signs of measles in any child all children who have been in contact with this child must be administered antimeasles serum or gamma-globulin.

For inoculations against measles, in cases of contact with patients, the blood serum of healthy adults (donors) or serum of placental blood collected at special stations is used. Gamma-globulin is administered for the same purpose; the dose is 3 ml for children 3-6 years of age and up to 10 ml for adults. Gamma-globulin inoculations have certain advantages over serum inoculations. The passive immunity conferred by inoculations lasts about 1 month.

RUBEOLA MORBIOLLOSA

Aetiology and epidemiology. The causative agent of the disease is a special filtrable virus. The disease usually affects children 4-10 years of age; it is an air-borne infection transmitted on close contact with patients. Patients are contagious from the last days of incubation until complete disappearance of the eruption from the skin.

Incubation period. In most cases the incubation period is 12-14 days, but may last up to 23 days.

Clinical picture. The disease sets in with a rise in temperature to 38.3-38.5 C, but sometimes persists at subfebrile figures. Some patients develop a mild rhinitis, cough and conjunctivitis. The patient's general condition is usually unaffected. At the end of the first day of the disease, sometimes on the second or third day, a roseolous micromacular eruption appears on the face and then rapidly (in the course of 24 hours) and without any definite succession spreads all over the skin; the eruption is not elevated above the surface of the skin. Simultaneously with the appearance of the eruption the occipital lymph nodes enlarge. Sometimes other lymph nodes may also enlarge. It should be remembered that usually not only the occipital lymph nodes palpated behind the mastoid process, but also the axillary and inguinal nodes *enlarge simultaneously*. The eruption lasts 2-3 days and then disappears leaving neither desquamation nor pigmentation.

Examination of the blood reveals leucopenia and during later periods monocytosis.

An attack of the disease confers lasting immunity.

Diagnosis. The disease is diagnosed on the basis of clinical symptoms and the blood picture. Special attention must be paid to the enlargement of the occipital lymph nodes, which will facilitate the differentiation of the disease from measles.

In cases where there are reasons to assume a diagnosis of measles and in doubtful cases where it is difficult to differentiate this disease from measles it is advisable to administer to the patient 2-3 ml of gamma-globulin or 30-40 ml of antimeasles serum and isolate the patient.

Treatment. Bed rest for 2-3 days without medicinal treatment.

Prevention. The patient must be isolated at home until seven days have elapsed since the disappearance of the eruption.

LETHARGIC ENCEPHALITIS (ECONOMO'S DISEASE)

Etiology. The causative agent of the disease is apparently a filtrable virus which selectively affects the central nervous system.

Epidemiology. The sources of the infection are only patients and carriers; the infection is air borne. The disease occurs mainly in countries with a cold and moderate climate; the maximum incidence of the disease is between February and April.

Pathogenesis. The characteristic disturbances in the organism are acute inflammatory processes in the central nervous system localized around the third ventricle, the cerebral aqueduct and the fourth ventricle, and developing in connection with the pathology of small blood vessels.

Early clinical signs. The incubation period is 5-6 days. As a rule, the disease sets in acutely with signs of general indisposition, adynamia, jadedness, headache, rise in temperature, accelerated respiration and tachycardia. The patients are usually irritable, their mood is unstable and the appetite is diminished. During this period the disease somewhat resembles influenza; within a few days all morbid symptoms disappear.

Clinical course. Within 8-10 days and sometimes only within a few months the disease enters the second period which is characterized by progressive symptoms of affection of the central nervous system. The duration of the second period varies with individuals, but may last several months (up to 1 year), while chronic forms (*parkinsonism*) last for years. It should be remembered that parkinsonism (see below) may be either the final stage of different clinical forms of the disease or a special form of chronic encephalitis.

The following forms are conventionally distinguished according to the course and symptomatology of the disease: lethargic, hyperkinetic and amyostatic (*parkinsonism*).

The most frequently occurring *lethargic* form of encephalitis is characterized by sluggishness, adynamia and sleepiness; the patient is likely to fall asleep under any circumstances. Considerable sleepiness is combined with sluggish facial movements, masklike, fixed face, and inarticulate, slurred speech.

The characteristic neurological symptoms of this disease are drooping of the upper eyelids (ptosis), unequal diameter of the pupils (anisocoria), squint (*strabismus*), double vision (*diplopia*), horizontal nystagmus, and convergence disturbances. These symptoms are determined by pareses and paralyzes of the muscles which are concerned in the movements of the eyeballs and in raising the upper lids.

The *hyperkinetic* form is marked by twitchings of various muscle groups (for example, the obliquus abdominis muscles), tremor of the hands, athetosis and other neurologic symptoms indicating predominant affection of the striopallidal system.

The symptoms of the chronic, *amyostatic*, form (*parkinsonism*) are constraint, rigidity of all muscles of the body, masklike face, characteristic gait, inarticulate speech, and tremor of the extremities and the trunk.

Diagnosis. Diagnosis of sporadic cases presents essential difficulties and must be based on epidemiological data and the entire clinical picture with particular consideration of the marked sleepiness of the patients and subsequently the inexpressiveness of the face (masklike face) and motor disorders.

Differential diagnosis. During the initial period the disease must be differentiated from *tuberculous meningitis* and *secondary encephalitides* associated with measles, smallpox, chickenpox and certain other infectious diseases (for example, typhus). The presence or absence of the most important symptoms of these diseases and an analysis of the symptoms with a definite suspicion of lethargic encephalitis make it possible to establish a correct differential diagnosis. In endemic foci of tick-borne and mosquito-borne encephalitis it is necessary to establish a careful clinical differential diagnosis making use of laboratory data.

Prognosis. In lethargic encephalitis the prognosis is doubtful in all cases because death may ensue as a result of rapidly progressing bulbar phenomena. An attack of the disease often leaves stable phenomena of parkinsonism.

Treatment. During the period of acute phenomena patients are hospitalized. In cases of convulsions and excitement the patients are administered starch-water enemas (100 ml) with chloral hydrate (1 g); symptomatic therapy is combined with a diet of semiliquid, easily assimilable food.

Patients affected with parkinsonism are given (with appropriate precautions) scopolamine and tropacine (ester of diphenylacetic acid hydrochloride) and are kept under medical observation.

Prevention. Revealmnt of patients, their immediate hospitalization, disinfection in the focus and the hospital where the patients are placed.

SMALLPOX (VARIOLA VERA)

Smallpox is an acutely infectious epidemic disease caused by a special filtrable virus; it is characterized by a two-wave temperature curve, considerable general intoxication and papulopustular eruptions on the skin and mucous membranes.

Brief historical information. Mass smallpox incidence was observed as far back as antiquity. Methods of smallpox prevention consisting in insufflation of smallpox crusts ground to a powder into the nose or in rubbing the same powder into the nasal mucosa were known in China eons ago. Devastating smallpox epidemics repeatedly attacked the people of Europe and other continents during the Middle Ages and modern times taking a toll of numerous human lives.

Variolation, i.e., immunization of humans by inoculation with the contents of human smallpox pustules, was extensively practised in the middle of the 18th century. However, this practice was fraught with the danger of smallpox infection since it consisted in administration of the living causative agent of smallpox.

In 1796 the English physician Edward Jenner used the contents of a skin pustule from a person affected with cowpox as inoculation material and thereby proved that the causative agent of cowpox passed through the human organism ("humanized" virus) may produce immunity without the danger of causing smallpox infection. Since the initial material was taken from a cow it was given the name of vaccine (*vacca*—Latin for cow). Later the vaccinations began to use detritus, i.e., matter scraped from the pustules on a calf's skin formed at the site of the scarifications into which the virus of a smallpox vaccine had been introduced.

At the end of the 19th century the Italian scientist Guarneri discovered in smallpox small inclusion bodies in the protoplasm of the epithelial cells; these inclusion bodies turned out to be products of the reactive change of the protoplasm in response to the penetration of the filtrable virus—the causative agent of smallpox.

Paschen's bodies, the elementary bodies discovered by E. Paschen in 1906 and found in the inclusion (Guarneri) bodies of smallpox, are now thought to be the virus particles which cause the disease (known as *Strongyloplasma variola*, var. *majoris*).

The inoculations against smallpox proved to be highly effective in the very first years of their administration (beginning of the 19th century). However, vaccination against smallpox was not compulsory in prerevolutionary Russia. smallpox incidence was high, very many people died of this disease and many of those who survived remained blind as long as they lived.

After the decree on compulsory smallpox vaccination passed by the Soviet Government in 1919 the incidence of the disease was sharply reduced, and soon smallpox was completely eradicated throughout the USSR.

Aetiology. The causative agent of smallpox is a special type of filtrable virus—*Strongyloplasma variola, var. majoris*. Microscopy of the contents of smallpox pustules stained with silver by M. A. Morozov's method reveals roundish Paschen's bodies which reach 0.2-0.25 μ in diameter. These elementary bodies are now considered the causative agents of the disease. It has been possible to see their fine structure by means of an electron microscope. The smallpox virus parasitizes intracellularly, but is also found in the pus of the pustules and in the smallpox crusts where it is retained for a long time. During the first days of the disease the smallpox virus is present on the mucous membranes of the nasopharynx and fauces. The causative agent long retains its virulence on desiccation and freezing, as well as in glycerin (if the external temperature is maintained at 5°C).

Epidemiology. Overall anti-epidemic measures with the most important part played by compulsory vaccination against smallpox have long since made it possible to eradicate smallpox throughout the USSR. Systematic vaccination against smallpox has also diminished the incidence of the disease in other countries.

Smallpox patients are the source of infection in all cases; they are contagious already at the end of the incubation period and during the first days of the disease when the infection is transmitted from a patient to a healthy person through the air; later the disease is transmitted through the matter contained in the smallpox pustules and the disengaged crusts. A certain role in the transmission of the infection is played by household utensils, toys and other things infected with the contents of the smallpox pustules or dry crusts disengaging from the skin or mucous membranes. The causative agent of the disease enters the human organism through the skin and mucous membranes. The *main* route of transmission of the smallpox infection is the air.

Clinical picture. The incubation period is 9-15 days. The disease sets in suddenly with chills and a rapid rise in temperature to 39.5-40.5°C (by the end of the second day). The onset of the disease is marked by pains in the small of the back, especially in the sacrum. These symptoms begin the earliest—*prodromal*—period of the disease, which lasts 3-4 days.

During the first two days the disease is accompanied by headache, dizziness, vomiting, loss of appetite and constipation. The pulse rate corresponds to the temperature level; some patients develop

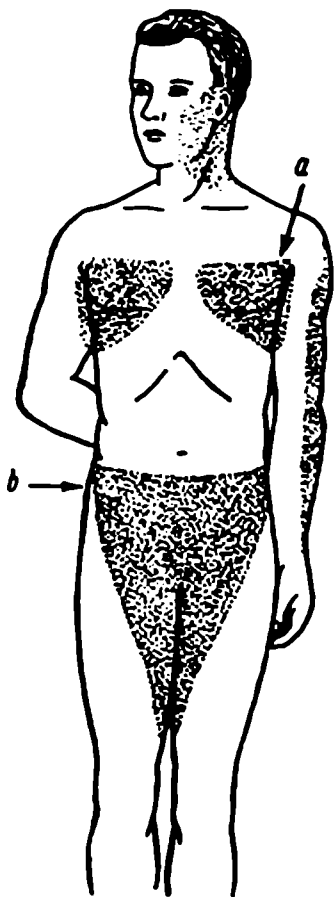


Fig. 86. Localization of the eruption during the prodromal period of smallpox

a—brachial triangle; b—femoral triangle

dyspnoea. Severe forms of the disease may involve loss of consciousness and delirium.

On the second or third day of the prodromal period some patients (25-30 per cent) may exhibit an eruption on the skin (prodromal eruption) which often resembles the scarlet fever or measles eruptions. The eruption appears on the medial surface of the thighs and the lower part of the abdomen (within the so-called femoral triangle formed laterally by the inferior medial parts of the thighs with the apex at the knee joints and the superior line connecting the anterior or spines of both ilia), on the superior lateral surface of both humeri (within the brachial triangle), on the extensor surfaces of the arms and partly on the neck and chest (Fig. 86); the

eruption lasts 2-3 days and disappears without leaving a trace.

During the prodromal period of smallpox the eruption usually consists of red macules or roseolas growing to the size of a lentil or even larger, or petechiae. There are also mixed forms of roseolous-petechial eruptions, especially in the brachial triangles.

The macular eruption breaks out mainly on the extensor surface of the arms, while the petechial and the mixed (maculopetechial) eruptions appear in the brachial and femoral triangles. At first the eruption of the prodromal period appears on the face and neck, and then in the brachial and femoral triangles.

According to a number of authors, the eruptions of the prodromal period of smallpox localized within the afore-mentioned triangles is particularly noticeable in women because of the absence of hair on their chests and thighs; the same eruption is also clearly seen in men who do not have very much hair within the area of its localization. Sometimes the eruption has no characteristic localization. At the end of the prodromal period the temperature falls and the patient's general condition improves. At the same time an

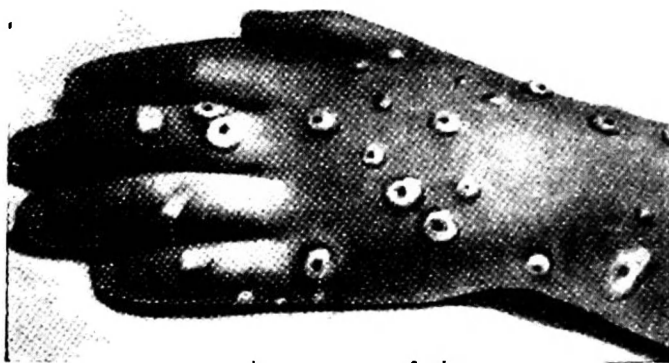


Fig. 87. Pustular pitted eruptions in child affected with smallpox

abundant ("true") micromacular smallpox eruption, its lesions slightly elevated above the surface of the skin, appears on the forehead, the scalp, face and hands. On the second day the eruption begins to spread to the trunk, and on the third day—to the lower extremities. The eruption which has broken out all over the body assumes the appearance of dark-red papules, after which a vesicle containing tissue lymph forms on the top of each papule. During the two days immediately following the vesicle enlarge to 3-4 mm in diameter; some of the vesicles become pitted (pock-marked) (Fig. 87). Externally the smallpox vesicles, pitted in the centre and filled with lymph, resemble pearls projecting from the skin. Each vesicle is surrounded by a narrow border of hyperaemia; the vesicle or the pustule to which the vesicle has given rise is divided into several cavities by partitions consisting of cell walls, has a dense base and is located on somewhat indurated, oedematous skin. When smallpox vesicles and pustules are punctured by a needle they do not collapse.

Particularly abundant eruptions break out on the forehead, face (Fig. 88) and the hands. The mucous membranes of the soft palate, pharynx, gums, nasal passages and conjunctivae are usually affected with similar lesions. Nasal respiration becomes difficult, and the patient develops photophobia, epiphora, hoarseness, a cough and salivation. The maceration of the epithelium of the oral and nasal mucosa is responsible for the fact that the vesicles easily develop into ulcers.

The successive transition of the papules to vesicles—stage of *fourthling* of the eruption—occurs on the 7th and 8th days of the disease in the order in which the eruptions appeared.

On the 9th day of the disease the temperature rises again and the disease enters the stage of *pustulation* (Fig. 89). This is the most distressing period.

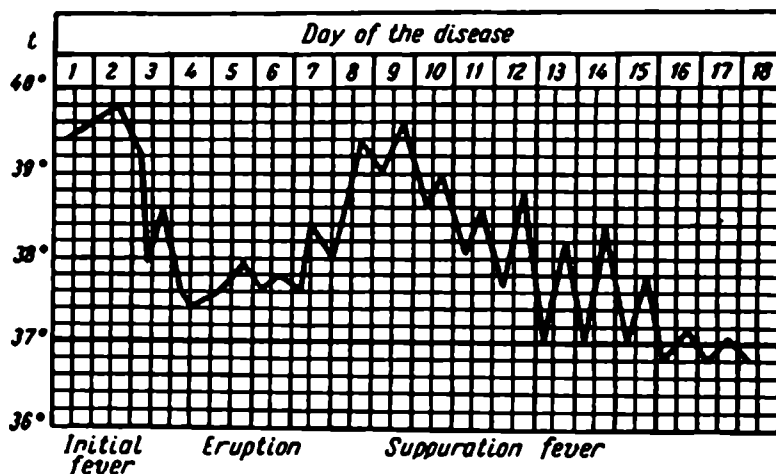


Fig. 89. Temperature curve of smallpox patient

During the days that follow the daily temperature variations amount to 1.5°C. The patient's general condition becomes much worse, and his consciousness is sometimes clouded; some patients become aggressive.

Lymph accumulates in the smallpox vesicles and their walls grow tense. The contents of the vesicles become turbid because of the pustulation, the vesicles acquire a yellow tinge and are transformed into pustules (Fig. 90) which do not run together even when the eruptions are abundant (*variola vera discreta*).

The red border surrounding each pustule grows bright-red and wider. In the area of the eruptions the subcutaneous tissue and the skin become swollen and the eyelids noticeably oedematous.

Owing to the formation of numerous pustules on the skin and mucous membranes the patient develops sharp pain in the parts which sustain the pressure of the body and tries to find a comfortable position in bed. Stretched by the matter accumulated in the pustules the thinned pustule walls easily burst and the pus is discharged to the exterior where it flows onto the skin and the underwear. The discharge of the pus onto the surface of the skin causes maceration of the latter and a sharp itching. The haemogram is characterized by neutrophilic leucocytosis. The irritation and oedema of the mucous membranes of the nasopharynx and fauces give rise to pain on swallowing, which makes the patients refuse food.

Respiratory difficulties, dyspnoea and sometimes even attacks of asphyxia caused by oedema of the larynx considerably aggravate the patient's condition. The intense itching of the skin causes distressing insomnia which still more aggravates the patient's condition.

On the 11th or 12th day of the disease the pustules begin to shrink and dry—beginning of the stage of *crust drying*. Starting on the



Fig. 5. Photomicrograph of a skin lesion (Vohra)

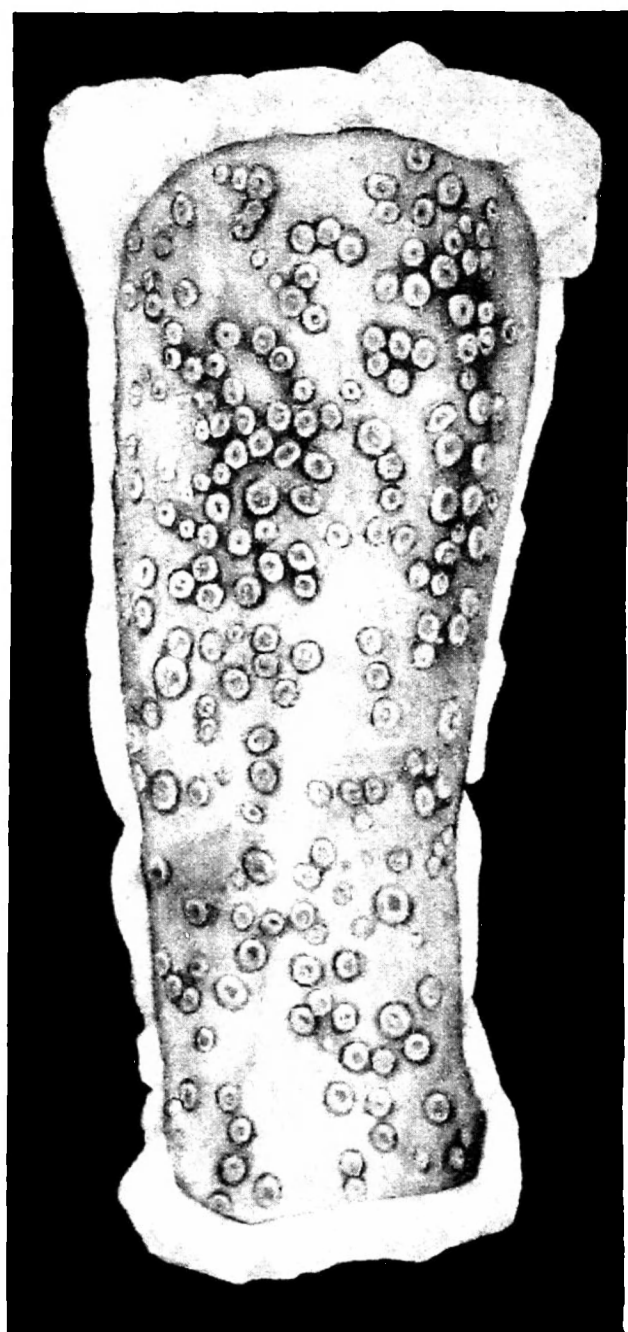


Fig. 1. Fossilized plant specimen.

face the pustules successively dry on the trunk and extremities, acquire a brown tinge and become covered with dry crusts.

As the inflammatory changes in the skin and mucous membranes gradually disappear the pains associated primarily with affection of the pharynx diminish, but the patients begin to be discomforted by intense itching and tear off the crusts under which bleeding and suppurating ulcers form.

The patients' general condition noticeably improves only after disappearance of the morbid symptoms on the skin and mucous membranes. About the 14th or 16th day of the disease the temperature returns to normal. After 18-19 days of the disease the crusts are gradually cast off at the sites where there were pustules and leave reddish macules which in time become brown, all over the body. Patients who have had deep pustular lesions on the face retain lifelong roundish scare (pock-marks). Pustular eruptions may cause corneal opacity and result in blindness.

In addition to the afore-described typical clinical picture of smallpox (*variola vera discreta*) there are numerous other forms of the disease.

One of the very rare but particularly severe forms of the disease is *purpura variolosa* which is characterized by a shorter incubation period (6-8 days), extreme toxicosis accompanied by circulatory insufficiency, and haemorrhagic diathesis. During the first hours of the disease patients develop sharp pains in the sacrum and a characteristic petechial eruption which is not confined to the afore-described triangles, but spreads all over the body. Numerous haemorrhagic macules appear on the skin in addition to the petechial eruption. The course of the disease is extremely aggravated by nasal haemorrhages, bloody vomit, haemoptysis, uterine and intestinal haemorrhages, haematuria, blood in the stool and early symptoms of cardiovascular disturbances. The patient may die even before the appearance of vesicles, between the 2nd and 14th days of the disease.

The disease is often accompanied by phenomena of necrotic laryngotracheitis and esophagitis. The spleen is not enlarged.

The blood picture is characterized by leucopenia or normocytosis, lymphocytosis, relative neutropenia with a sharp shift to the left - to myelocytes, basophils, plasmacytes and considerable thrombocytopenia (up to 7,000-6,500 thrombocytes per 1 cu mm of blood).

In *haemorrhagic smallpox* (*variola pustulosa haemorrhagica*) haemorrhage occurs into the vesicles and gives them a blackish appearance (*black smallpox*). The presence of blood in the sputum, vomitus, urine and faeces in this form of smallpox is due to haemorrhages into the mucous membranes.

The disease runs a very severe course, and death may occur between the 4th and 8th days of the disease.

In this form of smallpox the changes in the blood picture are

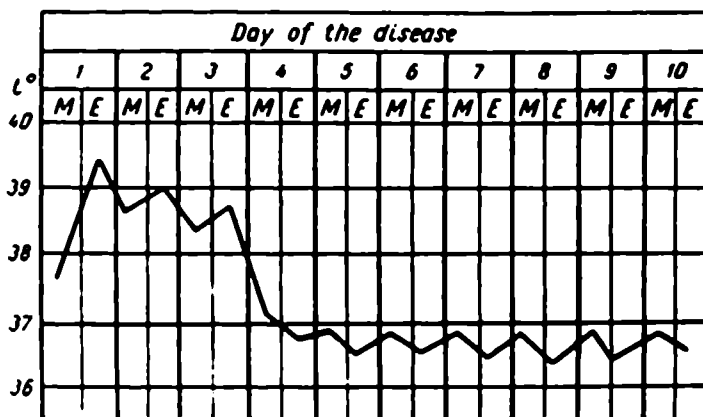


Fig. 91. Temperature curve of varioloid patient (author's own observation)

about the same as in *purpura variolosa*. There are also *intermediate* forms of smallpox—between haemorrhagic smallpox and *purpura variolosa*—in which, in addition to purpura, there are vesicular and pustular lesions.

In *confluent smallpox* (*variola confluens*) all of the skin (especially on the face and arms) becomes covered with an uncommonly abundant pustular eruption, the pustules spreading and running together; then extensive flat blisters filled with pus are formed. This form of the disease is characterized by a very high temperature, excitement and delirium. People surviving an attack of this disease retain large deforming scars on the skin.

There are also very **mild** forms of smallpox unaccompanied by a typical clinical **picture** of the disease. For example, *smallpox without an eruption* (*variola sine exanthematae*) takes place without a marked general reaction and eruptions and is therefore very difficult to diagnose (it may be diagnosed only by a careful analysis of the epidemiological data).

In countries where the population is systematically vaccinated and revaccinated mild, atypical and effaced forms of the disease are possible (upon appearance of an *imported* case of smallpox); these forms of the disease jointly classified as *varioloid* are very difficult to diagnose and may play quite an important role in epidemiology. The development of varioloid is accompanied only by part of the symptoms of typical smallpox. In varioloid elevated temperature (Fig. 91) lasts 2-3 days, the prodromal eruption is observed only in some cases and is not abundant, the patient's general condition is quite satisfactory, and true eruptions on the skin are limited to single lesions, most commonly on the forehead, face and neck (Fig. 92, patient on the right).

In varioloid the eruptions are limited to papules on a dense base

and their possible development into vesicles; as a rule, no pustules are formed and the lesions undergo rapid retrograde development without leaving a trace. All these characteristics of varioloid are associated with partial immunity of the organism. In varioloid the blood picture is characterized by leucopenia, a shift of the neutrophils to the left, relative lymphocytosis and presence of plasmacytes (up to 12-15 per cent) which appear on the 3rd or 4th day of the disease; eosinophilia is possible.



Fig. 92. Smallpox patient (left) and her 14-year-old sister affected with varioloid (from Schember and Kolmer)

Varioloid is rarely accompanied by complications.

Severe cases of smallpox are often accompanied by various *complications*, including bedsores on the sacrum, heels and occiput, gangrene of the oral and laryngeal mucosa, suppurative otitides, and concurrent secondary (coccal) infection with abscesses and phlegmons.

Focal pneumoniae, pleurisies, metrorrhagias and orchitides occur much less frequently in smallpox; as was already mentioned, affections of the cornea and iris may lead to blindness.

An attack of smallpox confers lasting immunity and reinfections are very rare.

Prognosis. Varioloid usually ends in complete recovery. The prognosis is also favourable in typical forms of smallpox (*variola vera*) unaccompanied by severe general phenomena or complications; however, lethal results are possible. Smallpox patients need special care and close watching.

Table 8

Differential-Diagnosis Table of the Main Signs of Chickenpox and Smallpox in Typical Cases

Symptoms	Chickenpox	Smallpox
1. Epidemiological anamnesis	Contact with a patient during the incubation period (up to the 21st day). absence of chickenpox in the anamnesis. Preventive administration of gamma-globulin makes the incubation period longer	Contact with a patient during the incubation period (up to 15 days), absence of vaccination or failure to keep to the revaccination schedule
2. Prodromal period	As a rule, the disease sets in gradually without prodromes. A small number of patients may have prodromal phenomena: chills, elevated temperature for 15-20 hours, vomiting, frequent semi-liquid stool, weakness, insomnia and loss of appetite In some cases, 1-2 days before the outbreak of true chickenpox eruption, a prodromal/eruption appears; it consists of punctiform and macropapular lesions, sometimes haemorrhagic purpura. The prodromal eruption lasts 10-48 hours and disappears without leaving a trace. Now and then enanthema is observed in the fauces	The disease sets in acutely with chills, sharp pains in the sacrum and lumbar region, vomiting, headache, anoxia and rapid rise in temperature to 39.5-40.5°C. Constipation and insomnia are observed. During the prodromal period 25-30 per cent of the patients exhibit macular, punctiform or mixed (maculopetechial) eruptions localized in the brachial and femoral triangles

3. Temperature during the period of true eruption	From the moment the true chickenpox eruption appears the temperature rises to 38.5-39°C. During additional outbreaks the rises in temperature are followed by several hours of remission owing to which the temperature curve is irregular. The febrile period lasts a total of 3-5 days (in uncomplicated cases) the temperature falling by accelerated lysis	The initial febrile wave corresponds to the prodromal period and lasts about 3 days; it is followed by 3-4 days of relative remission with the temperature falling to 37.3-37.4°C or to normal. The remission corresponds to the period of true eruption which is accompanied by an evolution of the lesions from macules (through papules) to vesicles. From the moment of pustulation the temperature rises again with big variations to 39.2-40°C
4. Localization of the eruption	True chickenpox eruption appears almost simultaneously on the face and scalp. Mainly the proximal parts of the trunk (for example, there are usually abundant eruptions on the back) and extremities are affected by eruptions. As a rule, there are no eruptions on the palms and soles	True smallpox eruptions are especially abundant on the peripheral parts of the body, mainly the hands and face (forehead). Eruptions are often observed on the palms and soles

The prognosis is usually more serious in cases of confluent smallpox (*variola confluens*). In haemorrhagic smallpox the prognosis is always very serious; cases of purpura variolosa are almost hopeless.

Diagnosis. The disease is diagnosed on the basis of a careful clinical examination of the patient and of epidemiological data. To diagnose smallpox during the initial period of the disease (1-3 days), it is important to consider the characteristic pains in the sacrum and the presence of prodromal eruptions in the femoral and brachial triangles; it should be remembered that the latter is observed only in 25-30 per cent of the cases of typical smallpox. Many patients vomit, lose their appetite and are afflicted with constipation. The pulse rate corresponds to the temperature level; some patients develop dyspnoea. Severe forms of the disease may be accompanied by loss of consciousness and delirium.

The diagnosis of smallpox is confirmed by the appearance of typical eruptions on the skin and mucous membranes on the 3rd day of the disease, especially by the character of evolution of the eruption (first a macule, then a nodule, papule, vesicle and pustule often pitted in the centre), and of the temperature curve (fall of the temperature from the 4th day of the disease and a new rise from the 9th day when the vesicles begin to pustulate), as well as by considerable general intoxication of the organism.

Owing to the certain resemblance of the eruptions to those of chickenpox, smallpox must be carefully differentiated from the latter disease. Due consideration must be given to anamnestic data, presence of sharp pains in the sacrum during the prodromal period of smallpox, the two-wave temperature curve, and morphological characteristics and sequence of the eruptions on the skin. It must be emphasized that, unlike chickenpox, smallpox is *often* accompanied by eruptions on the mucous membranes.

The symptoms of smallpox and chickenpox are compared in Table 8. The blood picture with the plasmacytic and thrombopenic reaction must be taken into account (p. 369).

In middle-aged and older people a diagnosis of chickenpox is extremely doubtful.

A *differential diagnosis* is particularly necessary when varioloid is suspected. It must be remembered that in varioloid the lesions are, unlike those in chickenpox, mainly uniform and that in chickenpox the appearance of the eruption is preceded by a rise in temperature.

If *purpura variolosa* is suspected, the disease must be differentiated from haemorrhagic capillarotoxicosis and severe manifestations of drug pathology caused by antibiotics and sulpha drugs.

In such cases it is necessary carefully to collect the anamnestic and all epidemiological data.

In some patients the eruption is of a morbilliform character and its early appearance on the face lends it a still greater resemblance

to measles. It must be remembered that measles is characterized by catarrhal processes (rhinitis, conjunctivitis, hyperaemia of the fauces, bronchitides), photophobia and Belsky-Filatov-Koplik sign (branny desquamation of the epithelium on the oral mucosa).

Scarlet fever (unlike the initial period of smallpox) is characterized by a saturated red of the transitional folds and bends of the skin (inguinal folds, elbow bends), presence of a nasolabial triangle free from punctiform eruption, and vomiting often observed during the first hours of the disease.

If the patient has an eruption on the skin and mucous membranes resembling that of smallpox, it is necessary to carry out the following complex of laboratory tests aimed at ascertaining the differential diagnosis of smallpox and chickenpox and of varioloid and cowpox. The laboratory tests require: (a) the discharge from the mucous membranes of the nasopharynx and oral cavity (mainly during the first 8 days of the disease), (b) contents of the papules, vesicles and pustules on the skin, (c) crusts and scales, and (d) the patient's blood.

For virological examinations the material is taken from patients with sterilized instruments into sterile glass containers. The pustular fluid, crusts, scales and detritus of the nodular pulp taken from the patient are placed separately in 5-ml glass ampules which are immediately soldered. The material may also be collected in sterilized test-tubes which have to be closed with sterile rubber stoppers.

The discharge from the nasopharynx is taken by means of sterile cotton tampons which are immediately thereafter placed in sterile test-tubes, the test-tubes being secured by sterilized rubber plugs.

The patient's blood is also tested virologically; 2-3 ml of the blood is taken (all rules of asepsis being observed) from a vein into a sterile test-tube containing an equal amount of distilled water; the test-tube is immediately stopped with a sterile plug.

To obtain smears of the discharge from the mucous membranes, a sterile cotton tampon is used, smears are made by the usual method on 4-5 slides and dried in the air.

The papules, vesicles and pustules on the skin are lightly painted with 92 proof alcohol and are punctured with a sterile needle at the base; the liberated drop is drawn into a Pasteur pipette.

In cases where it is impossible to collect the fluid from a nodule the soft pulp of the nodule is scraped with a scalpel. The detritus from the floor of a burst vesicle is also examined.

Before the viroscopic examination the contents of the smear on the slides are thoroughly triturated with a drop of physiologic solution until an opalescent emulsion is formed; the resultant suspension is examined for Paschen's bodies by using M. A. Morozov's method of silver staining, which makes it possible to differentiate smallpox from chickenpox.

An important role in the complex of smallpox laboratory tests is played by discovery of Guarnieri bodies formed in the rabbit's cornea, on the chorioallantois of a chick embryo or in a culture of tissues inoculated with the vesicular or pustular fluid containing the smallpox virus. Subinoculated in chick embryos the virus may in a number of cases be discovered only after the 5th or 6th passage.

If the results are negative, the chorioallantois being tested is triturated and a healthy chorioallantois of a chick embryo is inoculated with the resultant suspension for the second or third time. To differentiate the smallpox virus from the chickenpox virus, the chorioallantois suspensions are subjected to a haemagglutination test.

A haemagglutination inhibition test has been used of late for serological diagnosis of smallpox. As a rule, antibaemagglutinins are discovered in the patients' blood on the 5th or 6th day of the disease, although in low titres (for example, 1 : 80); by the 14th or 15th day their number reaches the maximum.

The laboratory diagnosis of smallpox may also be confirmed by a complement fixation test carried out in one of the two following variants: (a) during the first days of the disease in order to discover the antigen, and (b) at later periods in order to find complement fixing antibodies in the patient's organism (retrospective diagnosis).

It must be emphasized that neither the complement fixation test nor viroscopy using M. A. Morozov's silver staining method makes it possible to differentiate smallpox from the generalized form of cowpox (sometimes resulting from vaccination), but both techniques do make it possible to differentiate smallpox from chickenpox.

Treatment. No specific methods of treating smallpox patients have as yet been elaborated. An auxiliary role is played by antibiotics (including penicillin with streptomycin or levomycetin) which prevent the development of purulent processes that are possible in complications of smallpox with secondary (coccal) infection.

Some effect may be expected from hyperimmune serum or immune gamma-globulin in cases of their early administration.

All patients are subject to strict individual isolation. The attending personnel must wear gauze masks, covering the face and mouth, and rubber gloves. All of the dressing material used by patients and the tampons employed in swabbing the pustules must be burned.

At the sites of vesiculation and pustulation the skin must be painted, i.e., lightly touched, with a cotton tampon soaked in a 2 per cent potassium permanganate solution. The parts of the skin irritated by the pus oozing out of the pustules should be wiped with a tampon soaked in a 5 per cent potassium permanganate solution. To relieve the tormenting itching of the skin during the drying of the crusts, the latter are inuncted with a 1 per cent menthol ointment on a vaseline base.

The patients (especially children) must not remove the crusts because their removal leaves scars at the sites of the eruptions; to prevent this, the nails of adult patients must be trimmed, while the hands of children must be additionally bandaged to the trunk with a soft cotton padding in between.

To mitigate the pains, patients are usually given pyramidon, phenacetin and analgine. The cardiovascular function is supported with injections of a 25 per cent oil solution of camphor, a 5 per cent ephedrine solution and a 25 per cent cordiamine solution. The oral cavity of patients required special care; it must be swabbed with a cotton tampon moistened with a solution of glycerin and boric acid; the eyelids must be irrigated with a 2 per cent aqueous boric acid solution. A moist chloramine disinfection must be carried out at the patient's bedside.

Prevention. The following measures are extraordinarily important for preventing smallpox: earliest possible diagnosis of the disease, immediate hospitalization and strict isolation of patients, moist and gaseous disinfection in the focus and at the patient's bedside, 14 days of medical observation of all persons who have had contact with patients, and administration of preventive inoculations to all these persons. However, only systematic *vaccination* and *revaccination* make it possible to achieve decisive results in the prevention of smallpox, provided, of course, the aforementioned anti-epidemic measures are carried out.

Inoculations against smallpox are made with a *vaccine* containing living cowpox virus which differs from the smallpox virus in that it is nonpathogenic and yet capable of producing quite intensive immunity. The material used in inoculations is a detritus produced at special microbiological institutes.

To obtain the detritus, material containing the living cowpox virus is rubbed into the scarifications made on the shaven and disinfected skin of a calf. Within a few days vesicles and then pustules form on the calf's skin. The contents of these pustules are scraped off under aseptic conditions, and the detritus thus obtained is conserved in glycerin, the virus retaining its properties whereas the secondary (bacterial) flora dies off.

The detritus is dispensed in small, very thin, plugged glass tubes containing 20 inoculation doses. It must be stored in a cool (4°C) and dark place; the period of its storage is indicated on the label; if stored for a longer period, it loses its immune properties.

In 1951 the well-known Soviet virologist M. A. Morozov produced a *dry vaccine* with a longer storage period. Before inoculations the vaccine is dissolved in sterile glycerin (4 drops of glycerin for 20 inoculation doses of the vaccine).

Vaccination and revaccination with the detritus or the dry vaccine are carried out as follows.

The entire lateral surface of the shoulder is washed with soap and water and then thoroughly wiped with a piece of cotton moistened with ether; immediately after the skin has dried two drops of the dissolved vaccine are put on it 2 cm apart and scarifications with a Jenner vaccinator are made through the drops; care must be taken that the scarifications do not draw any blood. The skin is then allowed to dry for 10 minutes, after which the vaccinated person may dress. To preserve the sterility of the detritus and to use it economically, several persons are vaccinated or revaccinated at the same time.

A so-called vaccinal process develops on the skin at the site of the inoculation. Within 3-5 days a red macule forms at the site where the detritus has penetrated into the skin, the macule develops into a vesicle and the vesicle (from the 8th day) into a pustule. On the 11th or 12th day the pustule begins to shrink and a rather thin crust forms and soon falls off. Severe local reactions to the inoculation may sometimes occur.

Transfer of the contents of a vaccinal pustule to other parts of the skin results in *autoinoculation* (Fig. 93) with rather sharp and generalized manifestations in cases where the vaccinated person has had eczema, chafing or exudative diathesis.

According to law, *all* 9-10-month-old *Soviet children* are subjected to primary vaccination except those afflicted with acute infectious diseases. It should be remembered that, although the inoculations produce marked immunity, the latter must subse-



Fig. 5. Autovaccination in child vaccinated against smallpox

quently be renewed by *revaccination* at 4-5, 12, and 18-20 years of age.

In cases of direct danger of smallpox infection and during smallpox epidemics *general revaccination* is necessary regardless of age and remoteness of the last revaccination.

The high immunizing effect of the inoculations makes them the main and very reliable means of preventing smallpox.

ORNITHOSIS

Ornithosis is an acute infectious disease contracted from infected birds; it is accompanied by a febrile reaction and atypical pneumonia. The disease is caused by a group of filtrable viruses (*Rickettsiaformis ornithosis*).

In their biological properties these microorganisms are very closely related to the causative agent of *psittacosis*, a disease transmitted to man by parrots and related species of birds; the clinical picture of *psittacosis* closely resembles that of *ornithosis*.

Pigeons, ducks and stormy petrels, and much less frequently chickens, are the reservoir of *ornithosis* in nature. Man contracts the disease through close contact with birds; the infection is mainly air-borne. Workers of poultry farms and people breeding pigeons are most commonly affected. The signs of the disease in birds are refusal of food, conjunctivitis, suppuration in the eyes, and diarrhoea.

Symptoms and course. The incubation period in man is 7-15 days. The disease sets in acutely with chills, rapid rise in temperature and general indisposition. These symptoms are followed by dull pains in the chest and coughing with a very scant discharge of mucous sputum. The percussion and auscultation data manifested in a slight shortening of the percussion sound and single moist rales in the posterior inferior parts of the lungs are insignificant. The diagnosis of *ornithosis* therefore requires, in addition to the clinical picture, also a roentgenological examination of the chest supplemented by epidemiological and laboratory data. Roentgenoscopy and roentgenography of the lungs reveal small darkened areas indicating atypical pneumonia.

An attack of the disease confers rather lasting immunity, but the disease may run a protracted course.

Diagnosis. The diagnosis is based on epidemiological data (contact with birds infected with *ornithosis*), the clinical picture, roentgenology of the chest, positive results of a complement fixation test, and of an allergic skin test, for which 0.1 ml of a specially prepared *ornithosis* antigen is administered into the forearm strictly intracutaneously. The result of the skin test is read twice—in 24 and 48 hours; the test is considered positive if a hyperaemic macule at least 3×2.5 cm has formed at the site of the injection.

Treatment. All patients are hospitalized, although no cases of infection of healthy people by patients have ever been observed. The disease is effectively treated with blomycin or tetracycline in a dose of 300,000 U four times per day for 6-10 days until a stable clinical effect is produced, i.e., normalization of the temperature and liquidation of focal pneumonia.

Prevention. On poultry farms it is necessary to find and slaughter the infected birds (these birds must not be used for food); thorough disinfection with a 10 per cent chloride of lime solution must be carried out in the poultry yards. Analogous measures must be taken on finding infected pigeons. For contact with infected birds it is necessary to wear respirators or gauze masks.

Poultry-farm personnel working with ducks must strictly observe the rules of personal prophylaxis when symptoms resembling those of *ornithosis* appear in the birds.

ACUTE ANTERIOR POLIOMYELITIS

Acute anterior poliomyelitis (also known as *infantile paralysis*, *epidemic paralysis*, *acute wasting paralysis* and *Heine-Medin's disease*) is an infectious disease of the central nervous system caused by a filtrable virus. The disease is characterized by a short febrile period and catarrhal phenomena followed by pareses and flaccid muscular paralyses with predominant affection of the anterior horns of the grey matter of the spinal cord.

The first scientific description of the clinical aspects of the disease at the paralytic stage was given in 1840 by the German orthopedist G. Heine; in 1890 the Swedish physician K. Medin considerably supplemented the description of the clinical aspects of the disease. An important contribution to the knowledge of this disease was made by the well-known Russian pediatricist N. F. Filatov (1846-1902) in his detailed study of the clinical picture of the disease, while the neurologic status of patients affected with this disease was elaborated in detail as early as 1883 by A. Y. Kozhevnikov.

Aetiology. Acute anterior poliomyelitis is caused by a special type of filtrable virus (*Myelophilus hominis*) which penetrates into the cells of the central nervous system (brain and spinal cord) and the lymph nodes where it parasitizes. The existence of three serological types of virus (I, II and III), which do not produce cross immunity, has been established.

In culture the poliomyelitis virus is an elementary particle about 12-15 m μ in diameter; it stains violet by the Romanovsky-Giemsa method.

Heating kills the causative agent of the disease. Disinfectants also rapidly kill it, even in small concentrations. In brain tissue containing the poliomyelitis virus and placed in glycerin the virus long remains viable. Cold and even freezing but negligibly diminish the activity of the virus.

Methods of laboratory diagnosis have now been elaborated. The virus may be cultivated in a special nutrient medium containing a culture of human fibroblasts. Poliomyelitis may be experimentally produced in monkeys.

Pathogenesis and pathologic anatomy. After gaining entrance through the atrium of infection (oral cavity, intestines, nasopharynx) into tissue lymph the filtrable virus moves along the lymphatics of the cranial and spinal nerves to the central nervous system.

The virus similarly spreads, with the lymph, through the brain substance.

Pathohistological examination reveals diffuse inflammatory processes in the grey matter of the spinal cord at the level of the cervical and lumbar enlargements; anatomical changes are found mainly in the anterior horns of the spinal cord. Because of this the disease is called acute anterior poliomyelitis.

The cells of the anterior horns of the spinal cord undergo necrobiotic changes with cicatrization and shrinkage of the anterior horns. This gives rise to flaccid spinal paralyses and pareses which are in a number of cases irreversible. Virus-neutralizing antibodies accumulate in the patients' blood (humoral immunity).

Epidemiology. Poliomyelitis most commonly affects children up to 7 years of age, but it also attacks older children and is sometimes observed in adults. During epidemics the percentage of older children afflicted with the disease increases. The infection occurs mainly *through the intestines*, but it is probably also air-borne. Healthy people may be virus carriers. The main route of transmission of

the causative agent from patients to healthy people is enteral, for which reason most authors consider poliomyelitis an intestinal infection. We describe it in this part of the textbook because this part deals with children's infections and poliomyelitis affects predominantly children.

Poliomyelitis is mainly a seasonal disease: its incidence increases in July and August, especially in hot weather, and often reaches its maximum in September and October. In winter both sporadic cases and focal epidemics are observed.

In recent years poliomyelitis has occurred in the USSR in single cases and in numerically insignificant focal epidemics.

Clinical picture. The incubation period of poliomyelitis is from 2-6 to 25-26 days and in some cases up to 35 days.

It is now customary to divide the clinical forms of acute poliomyelitis as follows: (1). Nonparalytic poliomyelitis: (a) abortive form, and (b) meningeal form; (2). Paralytic poliomyelitis: (a) spinal form, (b) bulbar form, and (c) bulbopontine form (involving the pons).

As a rule, poliomyelitis sets in with a rise in temperature, headache, insomnia, dizziness, hyperaesthesia and a certain decrease in muscle tone; sometimes the onset is accompanied by vomiting and often by excessive sweating of the head, and pain in the muscles of the neck and the lower extremities. The subsequent course of the disease is determined by its concrete clinical form.

The *abortive* form of nonparalytic poliomyelitis is marked by a brief febrile period, headache and upper respiratory catarrh or dyspeptic disorders (more details below).

The *meningeal* form of nonparalytic poliomyelitis is characterized by elevated temperature for 6-7 days, insomnia, dizziness, hyperaesthesia and decreased muscle tone; meningeal symptoms and often vomiting are observed.

In some cases changes are found in the cerebrospinal fluid; elevated protein and pleocytosis in the cerebrospinal fluid are combined with meningeal symptoms.

Children often have peripheral-type pareses or paralyses of the facial nerve (Fig. 94).

Other patients affected with the same meningeal form of nonparalytic poliomyelitis do not exhibit clinically marked meningeal symptoms, although the cerebrospinal fluid shows changes characteristic of serous meningitis. The question of diagnosis is decided by isolation of the poliomyelitis virus from the patient.

Paralytic poliomyelitis which occurs in 2-5 per cent of all cases of the disease (the incidence of paralytic forms in proportion to the total poliomyelitis incidence varies, according to different authors, within very wide limits) may take place in one of the three aforementioned clinical forms.

The spinal form of paralytic poliomyelitis is the most frequent;

it affects mainly the extremities. The course of this form of the disease is described below.

The only neurologic manifestation of the pontine syndrome is affection of the facial nerve (including all its branches).

In its course paralytic poliomyelitis goes through a prodromal, preparalytic and paralytic stages.



Fig. 94. Paralysis of the facial nerve in child affected with poliomyelitis

The symptoms of the first stage are a change in the patient's general condition for the worse, headache, a slight rise in temperature and pain in the throat.

The preparalytic stage begins with dizziness, sleepiness, headache, nausea or vomiting; the temperature rises to 39-40°C, persists at that level for 4-7 days and falls to normal critically. A decrease in muscle tone of various groups of muscles is clearly observed.

The most characteristic symptoms of this stage are headache, hyperaesthesia and pains in different parts of the body (especially in the spine), paraesthesia and considerable sweating. The sleepiness may be so extreme that the patient is in a state of semistupor. The cerebrospinal fluid, flowing out upon puncture under elevated pressure, contains elevated protein and an increased number of cells (pleocytosis) with neutrophil leucocytes prevailing. In many cases the elevated protein in the cerebrospinal fluid fails to correspond to the rise in the cell count (*albuminocytologic dissociation*); subsequently the number of cells increases.

Symptoms of cerebellar dysfunction (vestibular phenomena) and nystagmus are often observed.

The drop in temperature is followed by development of flaccid paralyzes of the muscles of the shoulder girdle and arms (Fig. 95), thighs, shanks and trunk. The muscle tone in the affected muscles is decreased, the reflexes are diminished or absent. The paralytic period lasts 8-15 days.



Fig. 95. Paralyzes of upper extremities in acute anterior poliomyelitis

Paralytic poliomyelitis affects predominantly the proximal parts of the extremities; the zone of spread of pareses and paralyzes is at first very extensive (to the point of paraplegias); then the patient enters the next period—*restorative*—during which the active contractility and tone of a number of muscles are restored.

However, the motor functions are not always restored and not always completely; muscular paralyzes leading to muscular atrophy and development of permanent paralytic contractures (Fig. 96) are therefore sometimes retained during *the residual period*.

The bulbar form clearly involves the brain stem in the pathologic process. The most important signs of *the bulbospinal form* are deglutition disorders, inarticulate speech, choking (which is due to affection of the nuclei of the 9th, 10th and 12th pairs of cranial nerves) and peripheral pareses and paralyzes.

The abortive form of poliomyelitis is characterized by an acute onset with a rapid rise in temperature, headache, repeated vomiting, sleepiness, starting during sleep, and often a liquid faecal stool.

An attack of the disease confers lasting immunity.

Diagnosis. As was already pointed out, it is difficult to diagnose the clinical forms of poliomyelitis, in the absence of paralyzes.

but possible if all the afore-described clinical symptoms, epidemiological data and the season (summer and autumn months) are given careful consideration. An important part in establishing the diagnosis is played by a decrease in muscular power of at least some groups of skeletal muscles. An electromyogram (a record of the response of a muscle to electric stimulation) helps in establishing the diagnosis. Even feeble signs of muscular affection (drooping



Fig. 26. Paralysis of dorsiflexors of the right foot in acute anterior poliomyelitis

of the outward rotation of the leg, limping) must be taken into account. It is important to remember that poliomyelitis patients retain all forms of sensitivity, the sense of taste, in particular, remaining unimpaired.

In the presence of paralysis the diagnosis is comparatively simple. In poliomyelitis the cerebrospinal fluid is clear and contains a decreased number of cells (up to 150 cells per 1 ml) and elevated sugar (up to 80-90 mg%). The changes in the cerebrospinal fluid according to the periods of the disease have already been described.

Unlike *epidemic meningitis* patients, poliomyelitis patients rarely exhibit eye symptoms; their meningeal symptom complex is also **less clearly marked**; examination of the cerebrospinal fluid helps **to establish** a correct diagnosis.

When suspecting paralytic poliomyelitis it is necessary to take into consideration acute infectious *polyneuroradiculitis* which, unlike poliomyelitis, is accompanied by impairment of sensitivity.



Fig. 10. Encephalitis in child (see text).

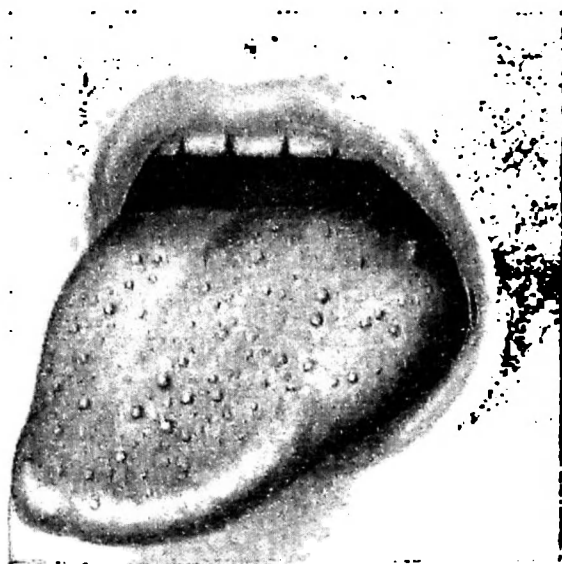


Fig. 99. "Raspberry" tongue in scarlet fever (3rd day of the disease)

Marked bulbar phenomena require *differentiation* of the disease from botulism and in some cases from rabies.

During the first days of the disease preceding the appearance of pareses and paralyzes it is often necessary to differentiate the disease from influenza (Table 9).

Laboratory methods of diagnosis. Isolation of the causative agent (filtrable virus) from the patient's organism (inoculation of mucus from the fauces, and of faeces) is the most reliable method of laboratory diagnosis; for this purpose the cytopathogenic effect is used (renal tissues of monkeys, fibroblasts of human embryos), in which case the development of the virus may be neutralized by a specific serum obtained by immunizing animals.

Of some importance are also the dynamics of the virus-neutralizing antibodies determined in paired serums at 5-day intervals between the tests; a 4-5-fold increase in antibodies is considered demonstrative.

Prognosis. Poliomyelitis is an infectious disease which constitutes a serious danger to life. In adults the disease runs a particularly severe course.

At least 15-20 per cent of the patients who have survived paralytic poliomyelitis retain lifelong paralyzes.

Treatment. All patients must be hospitalized. Bed rest is compulsory. The patients need an adequate diet of easily assimilable foods.

The patients must be prescribed vitamin C (0.6-1 g per day), gamma-globulin (0.35 ml per 1 kg of the child's weight per day), general roborant therapy, glutamic acid, and analgesics.

Treatment with proserine and dibazol (hydrochloride salt of a complex heterocyclic compound with benzene radical) contributes to restoring the functions of the nervous system and the locomotor muscles impaired by poliomyelitis. The doses of these drugs are prescribed in accordance with the child's age.

Dibazol is administered in powder form 3 times per day in the following doses: up to 1 year of age—0.001 g, 1-2 years of age—0.0015 g, 2-3 years of age—0.0025 g, 3-5 years of age—0.003 g, 5-9 years of age—0.004 g, and 9-12 years of age—0.005 g.

Proserine is administered in daily subcutaneous injections of an 0.05 per cent solution for 10-15 days. Children 3-5 years of age are administered 0.5 ml and 12-15 years of age—0.75-0.8 ml of the solution per day. In order to prevent contractures and spinal curvatures in cases of paralyzes the patients are placed on hard mattresses without pillows, the head resting on the mattress, legs extended. If a foot droops, it must be fixed in the normal position by a splint or adhesive tape.

These simplest orthopaedic measures must be carried out as soon as the patient is admitted to the hospital at the manifestation of even the earliest symptoms of affection of the locomotor functions.

Table 9

Table of Differential Diagnosis of Acute Poliomyelitis and Influenza

Symptom	Acute poliomyelitis (abortive form)	Influenza
1. Epidemiological anamnesis	The patient often turns out to have had contact with a poliomyelitis patient	Sometimes contact with an influenza patient is known for certain; during an epidemic the diagnosis is facilitated
2. Onset of the disease	Acute, but with short prodromal period	Acute, usually without a prodromal period. Mild chills often during the first hours of the disease
3. General condition of patient	Often grave. Adynamia is usually observed; excitement is less frequent; mild intoxication	Adynamia, jadedness; intoxication clearly marked
4. Consciousness	In severe cases clouded	As a rule, retained
5. Meningeal symptoms	Observed in a number of cases	
6. Local pains	Pains in nerve trunks and spine often observed. Headache only in some cases and localized in the occiput	Headache is a constant sign with predominant localization in the forehead, supraorbital arches and temples. Characteristic pain observed on movement of the eyes and pressure on the eye balls

‡ 7. Conjunctivitis, photophobia and epiphora 8. Cough and catarrhal phenomena in upper respiratory tract	Not characteristic and, as a rule, absent Occur in a small percentage of cases	Observed in 20-25 per cent of the patients Possible in 5-20 per cent of the patients
9. Phenomena of pharyngitis, feeling of stuffiness and scratching behind the sternum 10. Muscular tremor and diminished tone of different groups of muscles, sometimes with affection of the gait	Mild pharyngitis sometimes observed Frequent symptom	Characteristic and constant sign, especially in cases caused by virus A₂ Not observed
11. Sweating 12. Pulse and blood pressure	Moderate sweating of the head is characteristic Usually correspond to the temperature level (relative bradycardia possible in cases of bulbar phenomena)	Moderate sweating of all of skin is possible In most cases the pulse lags behind the temperature level. Blood pressure lowered

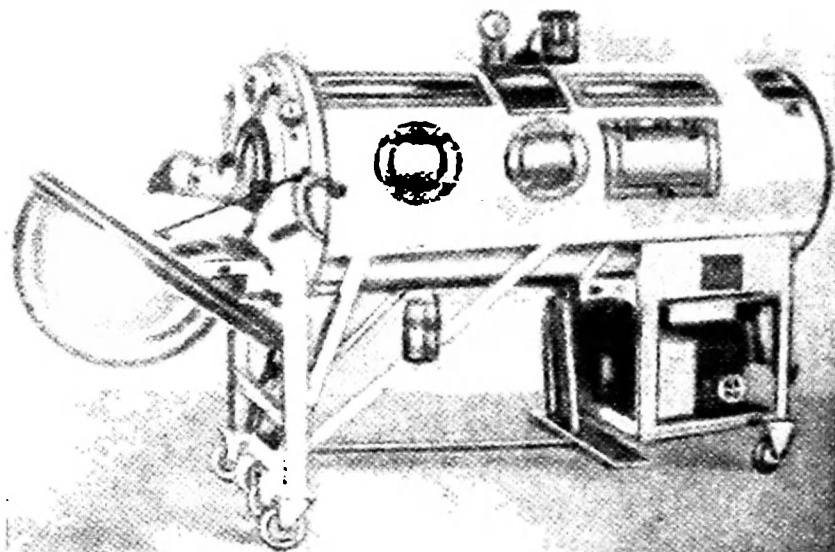


Fig. 97. Apparatus for artificial respiration

Immediately after the fall of temperature it is advisable to apply cold ray and UHF to the focus of the spinal cord affection in accordance with the segmental disturbance in muscular function. To improve the nutrition of the affected muscles and strengthen the function of the intact muscle groups, the muscles are subjected to cathodic electrization by faradic or galvanic current. These procedures must be supervised by competent personnel.

To restore the functions of the muscles affected by deep paresis physiotherapy, massage and kinesitherapy (active and passive movements) are used. Poliomyelitis patients must be watched by neurologists and orthopaedists; all physiotherapeutic procedures must be administered by experienced personnel. In cases of affection of the respiratory muscles a special apparatus for artificial respiration is used (Fig. 97).

When the acquired functions have been sufficiently fully restored (usually after the onset of the disease), pelotherapy and sea-bathing are recommended to consolidate the achieved therapeutic effects.

Stable deformities and contractures are corrected by orthopaedic operations.

Contagious hospitals must set apart special departments for the period of poliomyelitis epidemics. Patients who have survived paralytic forms of poliomyelitis must be placed in special wards of orthopaedic departments. Children with severe sequelae of paralytic

poliomyelitis must be sent to specialized children's institutions where school training is combined with work in shops.

Children who have survived paralytic forms of poliomyelitis need continuous medical observation in order that they may be given specialized physiotherapeutic and orthopaedic aid.

Prevention. Every poliomyelitis patient is subject to hospitalization and must be placed in a separate room or compartment.

During epidemics every child with elevated temperature, upper respiratory catarrh or diarrhoea must be put to bed at home and be kept under a physician's or assistant physician's observation for one week. Careful records must be kept of all cases suspected of poliomyelitis. All patients must be isolated for 40 days from the onset of the disease.

Upon appearance of a poliomyelitis case the focus must be thoroughly disinfected with all agents used in intestinal and air-borne infections. The patient's excreta (faeces, urine) must be mixed with dry chloride of lime (1 part of chloride of lime for 2 parts of the excreta) and dumped into the sewerage at least one hour later.

Rubber toys must be disinfected by soaking for 4 hours in a 3 per cent chloramine solution; other toys must be destroyed. The patients' handkerchiefs, towels and underwear must be soaked for 4 hours in a 3 per cent chloramine solution. The dishes and all other things used by patients must be disinfected by boiling. The patients' outer garments must be disinfected in formalin vapour chambers.

Persons who have had contact with patients are subject to a 20-day quarantine. Younger children (under 7 years of age) who have had contact with patients must be administered intramuscularly 50-60 ml of a healthy adult's whole blood or 6-15 ml of gamma-globulin. A vaccine from a killed culture of the virus is now prepared for active immunization (and is administered by special instructions). The effectiveness of Sabin's living poliomyelitis vaccine is now being tested in an extensive epidemiological experiment; the vaccine is administered per os in the form of a dragée containing the living modified poliomyelitis virus.

Soviet scientists M. P. Chumakov and A. A. Smorodintsev have improved the technology of Sabin's poliomyelitis vaccine production and have tested the vaccine on a large number of children. Their observations show that the vaccine is very effective and may be safely used for inoculations against poliomyelitis.

Upon the appearance of a poliomyelitis case in a children's institution, the group of children in which the case has been discovered must be quarantined for 20 days; transfer of children from, or admission of children to this group must be strictly prohibited.

Health education of the population and special training of the personnel of children's institutions play an important part in the prevention of the disease.

SCARLET FEVER

Scarlet fever is an acute infectious toxicoseptic disease accompanied by a febrile reaction, angina, enlargement of lymph nodes and punctiform eruption on the skin; it may occur at all ages, but is most frequent in children.

Aetiology. Despite the numerous studies carried out in the last 75 years the question of the aetiology of scarlet fever is still far from settled.

However, there can be no doubt that a haemolytic streptococcus plays a very important, although not the only, role in the aetiology of the disease.

The haemolytic streptococcus produces haemolysis when inoculated in Petri dishes containing blood agar. It is quite stable under unfavourable external influences; for example, it resists a temperature of 60°C for 2 hours, although it is killed by boiling in just 15 minutes; it is also stable under the action of disinfectants (mercury bichloride, carbolic acid, chloramine).

Epidemiology. Scarlet fever most commonly occurs in childhood, although it may attack adults who did not have it as children. The incidence of scarlet fever at a definite time and under definite conditions of a given community is determined primarily by the possibility of contact between patients and healthy susceptible people. The spread of the disease is favoured by overcrowdedness and violation of elementary rules of sanitation and hygiene.

The incidence of scarlet fever during the autumn and winter usually rises because of the catarrhal state of the nasopharynx, the lowered general resistance of the organism and the closer contacts among the children during the cold time of the year (indoor games, etc.).

Scarlet fever occurs mainly in countries with a moderately cold climate and high humidity; it is scarcely observed in hot countries.

Children under 1 year of age do not usually contract scarlet fever; children 6-11 years of age are the most vulnerable.

There are no scarlet fever epidemics in the USSR, and the incidence of the disease is limited to single (sporadic) cases and small local outbreaks as, for example, in a children's institution (nursery, kindergarten, school), if the first case has not been isolated in due time, no disinfection has been carried out and no quarantine has been established. The source of infection is a scarlet fever patient during the period of clinical manifestations of the disease and for the first 5-6 days after their disappearance. An important role in spreading the infection is played by children who have survived atypical and effaced forms of the disease.

Scarlet fever is an air-borne infection transmitted in droplets of saliva or mucus from the nasopharynx; healthy susceptible people may also contract the disease through third persons, under-

wear, various things and toys used by patients. The fauces and nasopharynx serve as the atrium of infection. The infection may also gain entrance through injured skin and mucous membranes (extrabuccal, traumatic scarlet fever).

In the largest cities of the USSR the period of isolation of scarlet fever patients has of late been considerably reduced.

Patients with the same date of onset of the disease are placed in one contagious department of a hospital. All patients hospitalized in a department at the same time are discharged also simultaneously between the 8th and 11th days of the disease on the basis of a sufficiently complete clinical cure and an acceptable blood picture. By this method it is possible to avoid mutual streptococcal infection of the patients who contracted scarlet fever at different times, but being hospitalized together found themselves in contact with each other with the possibility of transmitting the streptococcal infection to each other.

Pathogenesis and pathologic anatomy. In scarlet fever the primary affect localizes at the atrium of infection -the fauces and nasopharynx where angina (sometimes of a necrotic character) develops; it is accompanied by development of regional lymphadenitis which involves the submaxillary lymph nodes in the pathologic process. Scarlet fever is characterized by different degrees of necrotic changes in the tissues of the tonsils.

The development of the characteristic primary affect (anginal scarlet fever and submaxillary lymphadenitis associated with the affection of the tonsils), the manifestations of general intoxication of the organism due to the delivery of toxins from the tonsils, and certain septic factors determine *the first septicotoxic period* in the development of the disease, which lasts an average of about 3 weeks. In cases where penicillin treatment and administration of antistreptococcal serum are instituted early this period is considerably shortened.

In the third week the disease may enter *the second period* which is characterized mainly by allergic manifestations (nephritides, arthritides, lymphadenitides) with possible renewal of some of the symptoms of the first period (except the eruption and the toxicosis).

Scarlet fever may be marked mainly by toxic or septic phenomena which correspond to the pathoanatomic changes found at postmortem examinations.

The toxic form (or stage) of scarlet fever is characterized by an intense catarrh of the fauces and nasopharynx, toxicodegenerative changes in the central and vegetative nervous systems, and signs of protein and fatty degeneration in the myocardium and liver.

Pyoseptic processes prevail in the *septic form* (stage) of scarlet fever; purulent complications, such as diseases of the middle ear and the paranasal sinuses (otitides, mastoiditides, highmoritides, othmoiditides), are not infrequent.

A combination of toxic and septic components of the disease is most commonly observed in practice.

Clinical picture. The incubation period is 1-11 days (averaging 5-6 days). The disease sets in acutely; mild, but sometimes even intense, chills are followed by a rapid rise in temperature to 39-40.5 C; at the same time the patient is observed to vomit (once or repeatedly). The very first hours of the disease are accompanied by a headache, jadedness and pain on deglutition. Examination of the fauces reveals distinct hyperaemia of the soft palate, uvula and tonsils. The patient's somewhat puffy face is characteristic, the submaxillary lymph nodes are painful on palpation and somewhat enlarged.

From 22 to 24 hours after the onset of the disease (much less frequently during the first 2-3 days of the disease) a characteristic eruption breaks out in the form of numerous punctiform bright-red lesions located so closely to each other that they run together into a continuous field of hyperaemia.

The eruption appears first on the neck and the upper part of the chest; usually during the very first day of the disease (and much less frequently after 2-3 days of the disease) it spreads all over the body (Fig. 98). In typical cases the patients' cheeks are clearly hyperaemic, while the chin and the skin around the mouth are very pale (scarlatinal butterfly). The general intoxication of the organism and the focal changes in the fauces keep progressing during the first 3-4 days of the disease.

The tonsils become covered with a dirtyish-white or yellow-white film which may subsequently spread to the soft palate and the uvula with, in some patients, simultaneously developing necroses on the tonsils and enlargement of regional (submaxillary and cervical) lymph nodes. The appearance of the tongue in a scarlet fever patient is characteristic enough during the very first days of the disease. The tongue is moist and covered with a greyish-white film; from the 3rd or 4th day of the disease the film disappears, the tongue becomes scarlet-red (Fig. 99) and its tip shows numerous enlarged papillae (raspberry tongue).

The natural skin folds (in the elbow and inguinal bends) are of a saturated pink colour.

During the first 2-3 days the blood picture is characterized by neutrophilic leucocytosis, and from the 3rd or 4th day often by eosinophilia (up to 6-7 per cent). Usually the haemogram returns to normal during the first 8 or 10 days of the disease.

In ordinary uncomplicated scarlet fever the febrile period is 7-12 days. During the period of eruption the temperature rises still more and gradually returns to normal only after the eruption begins to fade. By this time the phenomena of anginal scarlet fever usually disappear.

The foregoing clinical picture characterizes the course of the

first period of scarlet fever. This period is followed by a period of convalescence or relative well-being of the patient, lasting till the 15th or 20th day of the disease when *the second period* of scarlet fever may set in; the second period is characterized by a number of complications (lymphadenitides, nephritides, otitides, etc.) many of which can be explained by sensitization of the organism to the streptococcus.

It will be observed that the second period of scarlet fever, especially with the modern methods of treatment using penicillin, antistreptococcal serum and other agents, does not usually occur or occurs very rarely.

After disappearance of the symptoms of the first period the patient's condition becomes quite satisfactory, and it is usually impossible to diagnose scarlet fever on the 8th to 10th days of the disease in view of the absence of clinical symptoms. Hence the necessity for establishing the diagnosis of scarlet fever in the very beginning of the disease in order that the patient may be isolated and all anti-epidemic measures in the focus may be carried out.

After disappearance of the eruption from the skin, sometimes somewhat sooner (even on the 6th or 7th day of the disease), a very characteristic, although late, symptom of scarlet fever—scaly desquamation of the skin—appears. The epidermis desquamating on the face and neck comes off in small scales, on the trunk (Fig. 100), back, thighs and buttocks—in considerable “shavings”, and on the soles, heels and palms—in massive layers. The scaly desquamation of the skin is particularly characteristic on the palms and soles. On the soles and heels it lasts 3-4 weeks. No desquamation of the skin is observed in penicillin-treated patients.

Typical cases of scarlet fever are distinguished as *mild*, *moderately severe* and *severe* (scarlet fever I, II and III), according to the severity of the course.

A considerable variety of scarlet fever manifestations may also be observed: from mildest, atypical cases to severe toxicoseptic cases which threaten the patients' life. In addition to dividing the cases of scarlet fever in accordance with the severity of the clinical course, it is customary to distinguish toxic, septic, toxicoseptic and effaced forms of scarlet fever on the basis of the peculiarities of the clinical picture. The first three forms are united by the general concept of severe scarlet fever since the presence of extreme toxicosis or septic phenomena is observed in severe forms of the disease.

In *the mild form* of scarlet fever the organism is very moderately intoxicated and the patient's condition remains satisfactory. The temperature does not rise above 39 C, and the febrile period lasts a total of no more than 5-6 days. Examination of the fauces in this form of the disease reveals catarrhal angina (without necrotic films); the eruption on the skin may be characteristic, but often has the appearance of indistinct lesions on the chest, neck and

inguinal regions. It must not be forgotten that in the mild form of scarlet fever complications, such as neuritis and lymphadenitis, may develop.

Toxic scarlet fever is characterized by an acute onset with repeated vomiting. In small children the consciousness is often clouded and convulsions are possible. Examination of the fauces shows intense hyperaemia of the tonsils. The eruption on the skin is very abundant and of a cyanotic character; haemorrhages (petechial lesions) are sometimes observed. The sclerae are saturated with blood, the pupils are constricted, the blood pressure sharply falls, the borders of the heart are extended and the heart sounds are considerably dulled. In the most severe cases with late treatment the patient may die during the very first 2 or 3 days of the disease. Death is caused by a severe toxic depression of the central nervous system and the cardiovascular apparatus.

The septic form of scarlet fever is marked by development of deep necroses in the fauces and the nasopharynx. The tonsils enlarge and grey necrotic films form on their surface. Purulent discharges from the nose are characteristic. The patient has an offensive breath due to the necrotic changes in the fauces. The regional lymph nodes (submaxillary and cervical) are enlarged and painful. The circulation of the streptococcus in the blood may give rise to various septic complications (suppurative otitides, pleurisies, arthritides). The temperature curve is of a septic, intermittent character.

The formerly observed *extrabuccal form* of scarlet fever in which the infection penetrates through injured skin or mucous membranes, for example, in burns, now occurs very rarely. In this form of the disease the eruption appears on the first or second day primarily around the atrium of infection; the temperature may rise considerably.

Complications. Owing to early penicillin treatment and administration of antiscarlatinal serum, and in large cities, additionally, due to simultaneous admission of patients, who have contracted the disease at the same time, to the same hospital department, complications of scarlet fever are now rarely observed.

The complications of scarlet fever during the initial period of the disease include *scarlatinal myocarditis* (extension of the heart borders mainly to the left, dull heart sounds, systolic murmur at the apex, arrhythmia; sometimes tumefaction of the liver, etc.).

Development of *scarlatinal nephritis* is observed during a late period of the disease (from the 20th to the 23rd day) and is manifested at first in general indisposition, nausea and vomiting. The patient's face becomes puffy, and the temperature often rises to 38.5-38.8°C. Examination of the urine shows it to contain protein and hyaline casts; the output of urine considerably decreases. As a rule, the blood pressure rises (it should be remembered that normally it is somewhat lower in children than in adults). In these

cases the prognosis is favourable; development of chronic nephritis is rarely observed.

If no appropriate measures are taken, individual patients with severe scarlatinal nephritis may develop uraemia, lose consciousness, and have convulsions and azotaemia. During the second period of scarlet fever (from the 21st to the 23rd day of the disease) patients may develop suppurative otitis and mastoiditis).

In cases complicated with otitis the temperature rises, the hearing in the affected ear is impaired, and pressure on the tragus of the ear is painful. The blood exhibits neutrophilic leucocytosis.

Complication of scarlet fever with mastoiditis considerably aggravates the patient's general condition, makes the temperature remittent, and disturbs the appetite and sleep. Pressure on the mastoid process is painful, and the blood shows neutrophilic leucocytosis.

Lymphadenitis, one of the most frequent complications of scarlet fever, may develop in the very beginning of the disease (in cases of anginal scarlet fever) or during later periods (3rd or 4th week of the disease). Usually the submaxillary, and anterior and posterior cervical lymph nodes are affected (they become somewhat hardened and painful), the temperature rises and the blood exhibits neutrophilic leucocytosis. As a rule, lymphadenitis is resolved, but sometimes it may suppurate, in which case pus is long discharged through the fistula that has formed or through the surgical incision.

The prognostic importance of any of the complications depends on the sum total of clinical data and the preceding physical condition of the patient. The disease is particularly hard to endure for debilitated and emaciated children.

An attack of the disease confers a certain degree of immunity, but relapses and reinfections are possible.

Diagnosis. In typical cases the diagnosis of scarlet fever presents no difficulties. In diagnosing the disease it is necessary to take into account the epidemiological data, acute onset (often with vomiting), sharply circumscribed hyperaemia of the tonsils, possible necrotic films on the tonsils, character of the eruption on the skin (punctiform eruption against the background of general hyperaemia of the skin, "saturation" of the skin folds), appearance of the tongue (particularly typical from the 4th or 5th day of the disease), enlargement of the lymph nodes and picture of the blood.

If the disease occurs in an effaced form, examination of all clinical symptoms and strict consideration of the epidemiological situation (contact with a patient) will help to establish the diagnosis.

In examining the patient's skin special attention must be paid to the hyperaemia and punctiform eruptions in the natural folds of the skin (elbow bends, inguinal folds).

Differential diagnosis. Scarlet fever must be differentiated from measles, rubella scarlatinosa, anginous-bubonic form of tularaemia, faucial diphtheria, various forms of erythema and drug eruptions.

The following symptoms speak in favour of the diagnosis of measles: prodromal period, Belsky-Filatov-Koplik's sign (branny desquamation of the oral mucosa during the first 3-4 days of the disease), marked catarrhal phenomena (conjunctivitis, laryngo-tracheitis), macromacular eruption elevated above otherwise unaffected skin and appearing in the following sequence over a period of 3 days (face, trunk, extremities), and leucopenia.

In rubeola patients prodromal phenomena are either absent or but moderate. On the 2nd or 3rd day of the disease all of the skin becomes covered with a pale pink macular eruption; the temperature rises very insignificantly. There are no symptoms of angina. The most characteristic sign of the disease is enlargement of the occipital and posterior cervical lymph nodes.

In some cases it is necessary to differentiate scarlet fever from faucial diphtheria. Diphtheria is marked by dense greyish-white membranes on the tonsils hardly removable from the underlying tissue. Scarlet fever is characterized by distinct hyperaemia of the fauces, which sharply separates the fauces from the unaffected surrounding mucosa, superficial necrotic films on the tonsils, and enlargement of the submaxillary lymph nodes with no oedema of the cervical subcutaneous tissue.

Follicular angina is noted for several large yellow equal-size islets on the tonsils (the islets do not spread beyond the tonsils), a considerable rise in temperature (39-40°C) and absence of any eruptions on the skin.

Drug erythemas, as a complication caused by antibiotic treatment, may be diagnosed by similar signs and on the basis of anamnestic data, for example, treatment of the patient with synthomycin to which the patient was particularly sensitive. Drug eruptions are characterized by appearance of macropapular lesions often arranged symmetrically and sometimes running together (confluent).

A careful analysis of all the data makes it possible either to confirm or exclude the diagnosis of scarlet fever.

Treatment and care. Upon establishment of the diagnosis of scarlet fever or upon suspicion of this disease the patients are placed in contagious department of hospitals.

The patients' skin must be kept absolutely clean, for which reason they must be bathed every 4-5 days; in severe cases the patients are given rubdowns. It is necessary continuously to watch the patients' oral cavity and make them gargle the mouth 3-4 times a day with a 2 per cent boric acid solution; the fauces of small children must be syringed with physiologic solution.

Since the initial period of scarlet fever is accompanied by development of angina, patients must be prescribed a diet of semiliquid food—mucilaginous soups, thin porridges, sour milk, jellies, stewed fruit, and preserves. The diet must contain enough vitamins.

Intramuscular injections of penicillin for 4-5 days are recommended from the very first days of the disease (especially in very severe cases and in cases of a septic process). The doses of penicillin must be prescribed individually in accordance with the patient's age and the severity of the disease. Children must be administered 100,000-500,000 U of the antibiotic per day; the course of treatment is 5-7 days and, if need be, longer.

Patients with the toxic and septicotoxic forms of scarlet fever must be administered, as early as possible, 10,000-30,000 U of antitoxic antiscarlatinal serum in accordance with the severity and period of the disease and the patient's age. The serum must be administered either by Besredka's method or by the method described on page 75. In cases of continuing toxicosis the serum injections are repeated during the 2 or 3 days immediately following.

Good results are produced by combined treatment with penicillin and antitoxic serum. In cases of marked cardiovascular dysfunction patients must be given cordiamine (per os and by injection) and in more severe cases—injections of camphor and ephedrine.

In caring for patients it is necessary to pay special attention to their ears, lymph nodes and joints, and from the 12th or 13th day of the disease—regularly to check up on the urine.

During the first two or three days following the appearance of symptoms of nephritis the patients must be prescribed a diet consisting of 150-200 g of sugar dissolved in 400-500 ml of tea or water and 100 g of white bread or zwieback.

Subsequently the patients must be transferred to a dairy and vegetable diet, including sour milk, curds, mashed potatoes, white bread and fruit, and very limited amounts of salt and liquids. It is also necessary to check as closely as possible on the consumption of liquid and the output of urine, making a urinalysis every 3-4 days. The patients must be kept strictly in bed and allowed out of bed only after disappearance of the oedema and normalization of the urine. But even after discharge from the hospital patients must keep to the diet for another 2-3 weeks.

Patients must have warm beds; application of heat to the feet is advisable.

Purulent complications of scarlet fever (otitides, mastoiditides, lymphadenitides) are treated according to the rules of surgery with administration of sufficiently large doses of penicillin.

Before discharging patients from the hospital it is necessary carefully to examine their fauces, nasopharynx and ears, and make a final control urinalysis.

Prognosis. At the present time scarlet fever runs, as a rule, a favourable course, although severe cases of toxic or septic forms of the disease may now and then be observed.

Early administration of penicillin has sharply reduced the number of complications.

If treatment is started in due time, the patient is kept in bed and adheres to the requisite diet, the prognosis is usually good. In some of the penicillin-treated cases (up to 2-3 per cent) reinfection is possible.

Prevention. The most important measures to prevent scarlet fever are early revealment and isolation of patients, and establishment of a quarantine in children's institutions (nurseries, kindergartens, children's homes, young pioneers' camps) where cases of the disease have been discovered. Children who have had contact with a patient must be kept out of children's institutions for 7 days after the contact.

Special attention must be devoted to revealing atypical and effaced cases of scarlet fever because of the very great epidemiological importance of these forms of the disease.

If patients who have contracted the disease at the same time are hospitalized simultaneously, they may be discharged on the 10th or 11th day of the disease, the blood picture permitting and provided they have sufficiently recovered clinically. But, if the patients have been hospitalized at different periods, they may be discharged only on the 40th day of the disease.

EPIDEMIC CEREBROSPINAL MENINGITIS

Epidemic cerebrospinal meningitis is a general acute infectious disease characterized by a stormy onset, high temperature, predominantly purulent affection of the meninges in which the causative agent lodges, and marked nervous symptoms.

Aetiology. The causative agent of the disease is the *Meningococcus Weichselbaum* or *Neisseria meningitidis* discovered in 1885. The meningococcus consists of two individuals (it is a diplococcus) resembling coffee beans turned to each other with their concave surfaces. The microbe stains well with methylene blue and fuchsin.

Typical epidemic meningitis occurs only in humans and cannot be fully reproduced experimentally. The meningococcus lodges in the pia mater of the brain and partly of the spinal cord, penetrates into the cerebrospinal fluid and localizes in cells. It is also found in mucus of the fauces and the nasopharynx.

In pure culture the meningococcus is grown on broth with an addition of blood serum or ascitic fluid, and on blood agar.

In the external environment the meningococcus is rather unstable, but in the mucus discharged from the throat of patients or carriers of the infection it may persist for a long time.

The existence of four serological types of the meningococcus (A, B, C and D) differing in their antigenic pattern has been established.

The virulence of the meningococci isolated from patients or carriers varies within rather wide limits.

Epidemiology. In the 19th century devastating epidemics of this disease often occurred. The last 20 years have seen a sharp decrease in the incidence of epidemic meningitis. Only single cases of this disease are now observed in the USSR.

The role of the source of infection is played by epidemic meningitis patients and healthy carriers. The spread of the disease is favoured by overcrowded housing conditions and congestion of the population.

The certain seasonal prevalence of the disease (March-April) is due to the fact that the nasopharyngeal catarrhs in healthy people facilitate the penetration of the causative agent through the mucosa of the lymphatic ring.

Epidemic meningitis is an air-borne infection and is transmitted through minute droplets of mucus containing meningococci being sprayed into the external environment from the nasopharynx and fauces of a patient or carrier.

Timely revealment and hospitalization of patients, and rational therapy (penicillin, norsulphazol) have sharply reduced bacteria-carrying.

Pathogenesis and pathologic anatomy. After gaining entrance into the human organism through the nasopharyngeal mucosa the meningococci spread along lymphatics in the direction of the meninges. Meningococci may also be carried from the atrium of infection to the meninges by the blood. In the meninges of the brain and spinal cord the meningococci find the most favourable conditions for their existence and multiplication.

As the disease develops, the pia mater becomes turbid and full-blooded; this is particularly noticeable at the base of the brain, where the meninges are impregnated with yellowish-greenish pus (basilar meningitis).

Postmortem examination of people who have died of epidemic meningitis reveals that the ventricles of the brain are also filled with pussy cerebrospinal fluid. The most important symptoms of the disease are associated with affection of the meninges and general intoxication of the organism. The abundance of neurologic symptoms in epidemic meningitis is due to the fact that the inflammatory changes in meninges affect the trunks of cranial nerves emerging from the cerebral hemispheres.

The organism overcomes the infectious process mainly through phagocytosis of the meningococci by leucocytes.

Bacteria-carrying which sometimes develops after an attack of epidemic meningitis is favoured by catarrh of the mucous membranes of the nasopharynx and upper respiratory tract.

Clinical picture. The incubation period averages 3-4 days, but may last from 2 to 7 days.

As a rule, the disease sets in acutely with chills, which are followed by a rapid rise in temperature up to 40-41°C, sharp headache

and vomiting (sometimes repeated). During the hours immediately following, the headache grows more intense and becomes tormenting. Herpes develops on the lips and at the wings of the nose from the second or third day of the disease.

In some cases the disease begins with a prodromal period which lasts 1-2 days and is characterized by indisposition, weakness, excess perspiration, mild headache and arthralgia. However, an acute onset is more frequent. The onset is often accompanied by motor unrest, clouded consciousness, delirium and stupor. Some patients develop convulsions. Cutaneous hyperaesthesia and photophobia are quite characteristic. The tendon reflexes may intensify or diminish.

In cases of retained consciousness the patients complain mainly of a sharp headache. The symptoms which are of diagnostic importance include those indicating affection not only of the meninges, but also of the brain and cord substance (pareses and paralyzes of the skeletal muscles and of the cranial nerves—meningomyelitides and meningoencephalitides). Stable red dermographism is often observed.

The specific features of the clinical picture of the disease are due to the meningeal syndrome.

The pathologic symptoms of affection of the nervous system become clearly marked within 20-30 hours of the disease. The occipital muscles become *rigid* because of the affection of the meninges (the patient cannot touch the chest with his chin when attempts are made to flex his head during examination). Kernig's sign (an attempt completely to extend the leg at the knee with the thigh flexed at a right angle causes pain or meets resistance; the same sign may be produced by an attempt to flex the thigh with the leg completely extended at the knee) is also characteristic.

Brudzinski's neck sign (passive flexion of the head is followed by flexion of both thighs and legs) is also frequent. The knee and Achilles tendon reflexes are often diminished.

Younger children assume a very characteristic pose—they lie with head and spine overextended and legs flexed at the knees (Fig. 101). Children often exhibit clonic and tonic spasms of muscles. Adults also often assume a forced position in bed—the head is overextended and the thighs are flexed.

Instead of the foregoing meningeal phenomena children 4-6 months old may show the following symptoms: restlessness, crying, bulging of the fontanels.

Sometimes symptoms are observed, which indicate affection of cranial nerves, including disturbance in the oculomotor function and *anisocoria* (inequality in the diameter of the pupils). The patient may develop convergence disturbances and inability normally to abduct or adduct the eyes, which is mainly due to affection of the 4th, 5th and 6th pairs of cranial nerves. If this disturbance is in-



Fig. 100. Scaling of the skin in scarlet fever



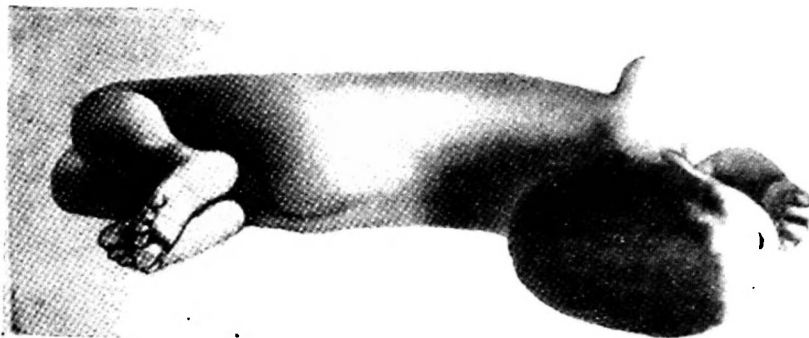


Fig. 101. Child affected with epidemic cerebrospinal meningitis

tense, strabismus is observed. On the side of the affected right or left oculomotor nerve the dilated pupil poorly reacts to light—its accommodation is disturbed; infrequent winking is characteristic; sometimes horizontal nystagmus is noted (oscillatory movement of the eyeballs).

The foregoing pathologic symptoms usually increase for 2-3 days and then become stabilized.

A lumbar puncture shows a turbid fluid, often markedly pussy, flowing through the needle under elevated pressure, i.e., in frequent drops or in a stream. The total protein in the cerebrospinal fluid is considerably elevated (0.6-4%).

The cerebrospinal fluid contains a large number of neutrophil leucocytes and meningococci many of which are engulfed by leucocytes and are found in the cells in a certain stage of phagocytosis.

Pandy's and Nonne-Apelt's tests are positive. During the first two days of the disease the fluid may be clear, but with an increased neutrophilic cytosis. In cases given early antibiotic treatment the cerebrospinal fluid may show no changes, which renders the diagnosis of the disease much more difficult.

The temperature persists at high figures for 5-7 days, but sometimes temporarily falls (for 1-2 days).

The encephalitic form observed mainly in young children is characterized by loss of consciousness, muscular spasms and deep pareses of various groups of skeletal muscles; meningeal symptoms are feebly marked.

The abortive form has a short febrile period, and all the main manifestations of the disease disappear quite soon despite the characteristic onset and a number of typical clinical symptoms of meningitis. During the very first 2-3 days of the disease the temperature drops to normal, the meningeal symptoms disappear, and the cerebrospinal fluid returns to normal within another 2-4 days.

The rudimentary form is characterized by feeble clinical manifestations of the disease, moderate febrile reaction and insignificant changes in the cerebrospinal fluid.

In patients treated with penicillin from the first or second day of the disease the clinical symptoms of meningitis do not appreciably develop and quite soon disappear, but the disturbances in the cerebrospinal fluid and in anatomic structures are eliminated later than the other very important manifestations of the disease.

In the absence or in cases of inadequate treatment *protracted* and chronic forms of the disease are observed; they occur in the following two principal clinical varieties.

The first variety may last up to 1.5-2 months with alternating exacerbations and remissions, considerable general malnutrition and apathy. Despite the protracted course the disease ends in the patient's recovery. However, severe disturbances in auditory acuity, persistent headache, impairment of memory and of the mental faculties are possible.

The second variety of protracted epidemic meningitis (usually in children) gives rise to *hydrocephalus* as a result of inflammatory changes in the ependyma. In such cases the production of cerebrospinal fluid by the vascular plexus increases and its resorption decreases.

Thus development of hydrocephalus is based on ependymitis—inflammation of the vascular plexuses of the lateral ventricles of the brain.

The symptoms of ependymitis, which develops between the 18th and 22nd days of the disease, are clouded consciousness, increased muscle tone, sluggish reactions of the pupils to light, strabismus and nystagmus. The complication develops mainly in cases of late treatment. Subsequently the patient's small and lateral fontanels begin to be palpated, the cranial sutures part and the head noticeably enlarges, which attests the development of hydrocephalus. The symptoms of hydrocephalus may disappear, but in some cases stable hydrocephalus develops and leads to cerebral exhaustion, general loss of intellect (to the point of feeble-mindedness) and a number of severe neurologic symptoms due to compression of the cerebral substance (deafness, blindness, deaf-mutism).

Sometimes epidemic meningitis runs a *fulminating* course and is accompanied by considerable general intoxication of the organism, loss of consciousness, convulsions and delirium. The patient may die before developing meningeal phenomena. In these cases there are haemorrhages into the adrenals and oedema of adrenal tissue, which lead to functional insufficiency (Waterhouse-Friderichsen syndrome); to bring the patient out of his extremely grave condition, it is necessary to administer cortisone (prednisone or prednisolone), intravenous drip infusion of physiologic solution, in-

intramuscular injections of 1 ml of a 5 per cent ephedrine hydrochloride solution 3-4 times per day, and massive doses of ascorbic acid (up to 800 mg per day). In doing this it is necessary to keep tabs on the potassium, sodium and sugar in the blood and sugar in the urine.

A peculiar form of meningococcal infection is *meningococcaemia* which is a sepsis produced by meningococci. The disease sets in acutely with chills and a rise in temperature to 39-40°C. Within 24 hours roseolous, papular and haemorrhagic eruptions appear on the skin of the lower extremities and the face. The lesions are of various sizes and forms—from small pinpoint haemorrhagic lesions to large red stellate macules; necrosis sometimes develops in the centre of these macules. Nasal haemorrhages are frequent.

Meningococcaemia is also accompanied by affections of the ankles and wrists and the interphalangeal joints of the fingers. Haemorrhages into the skin and apoplexy of the adrenals are possible.

In most cases of meningococcaemia there are no meningeal phenomena; the meninges may become involved only during the later course of the disease.

Three main typical clinical forms of the disease are customarily distinguished: *mild*, *moderately severe* and *severe*.

Complications. One of the most serious and stable complications is hydrocephalus whose symptoms were described above.

In patients suffering from cachexia, especially in childhood, epidemic meningitis may become complicated by development of otitis, pneumonia, purulent pleurisy and bedsores. Individual cases may become complicated by focal or diffuse nephritis.

Prognosis. In the past, before streptocide was used in the treatment of epidemic meningitis (before 1935-1937) mortality from this disease reached 40 per cent. Now, owing to the use of antibiotics, lethal results are extremely rare; complications have also become infrequent. The prognosis largely depends on the time the treatment is instituted and its correctness. An attack of the disease confers lasting immunity.

Diagnosis. The disease is diagnosed mainly on the basis of the clinical picture, epidemiological data (time of the year, contacts with patients or carriers) and examination of the cerebrospinal fluid. An acute onset with chills, vomiting and a rapid rise in temperature, rapid development of meningeal and other neurologic phenomena, and neutrophilic leucocytosis with a shift to the left speak in favour of the diagnosis of epidemic meningitis. The question of diagnosis is finally settled after a lumbar puncture and examination of the cerebrospinal fluid. In epidemic meningitis the fluid flows out under elevated pressure, is turbid and contains an excess of protein; microscopy of stained preparations reveals a large number of segmented leucocytes and meningococci partly in some stage of phagocytosis. Pandy's and Nonne-Apel't's tests are positive.

The precipitate of cerebrospinal fluid obtained on the bottom of a centrifugal test-tube after centrifuging is used for preparing smears on slides; the smears are stained by Gram's method and with methylene blue after which they are examined under the microscope. In the preparation the number of meningococci varies from single individuals to numerous microbial cells which resemble coffee beans turned to each other with their concave surfaces and located both inside cells (in polymorphonuclear leucocytes) and outside of cells. It should be noted that sometimes, even when the diagnosis of epidemic meningitis leaves no doubts, it is impossible to find the causative agent in the cerebrospinal fluid; this usually applies to patients who early began to be treated with antibiotics.

Two test-tubes containing ascites-broth are taken for bacteriological examination and 0.5-1 ml of cerebrospinal fluid is inoculated in them (it is best to inoculate the precipitate obtained by centrifuging the cerebrospinal fluid). The test-tubes with the inoculations and the remaining portion of the cerebrospinal fluid are placed in a thermostat for 18-48 hours at 37°C; if no growth is obtained, the remaining part of cerebrospinal fluid is analogously inoculated on ascites-broth in two other test-tubes. In positive cases the growth on broth is homogeneous; smears are prepared from the contents of the test-tubes, are stained by Gram's method and are examined under the microscope.

Bacteriological examination also includes inoculation of portions of cerebrospinal fluid precipitate (0.5-1 ml) on a Petri dish containing ascites-agar (Levintal's medium); after 18-24 hours of growth in a thermostat at 37°C very small greyish colonies form on the surface of the nutrient medium; stained smears are prepared from these colonies. After washing the isolated diplococci with physiologic solution the diplococci are tested for agglutination in test-tubes with specific diluted rabbit serum (it should be remembered that there are four serologic types—A, B, C and D—of meningococci).

In patients treated with intramuscular injections of penicillin, especially in cases of endolumbar administration of a sodium salt of penicillin, meningococci are rarely discovered in the smears or isolated from the cerebrospinal fluid.

Differential diagnosis. Epidemic meningitis must be differentiated primarily from tuberculous meningitis which is characterized by a gradual onset, rather slow rise in temperature, absence of leucocytosis, and a number of peculiarities in the cerebrospinal fluid (it is clear or slightly opalescent and, if allowed to stand in a test-tube for 20-24 hours, it becomes covered with a delicate film of fibrin containing lymphocytes). It is also marked by characteristic outcries of patients and slow fading of consciousness. Of course, all this applies to cases where no treatment for tuberculosis has been administered.

Modern agents used in the treatment of tuberculous meningitis (streptomycin, PAS, phthivazide [isonicotinic acid hydrazide derivative]) are, as a rule, sufficiently effective, arrest the progress of the pathologic process and contribute to its earliest termination.

Pneumococcal meningitis and purulent meningitis (caused by Pfeiffer's bacillus) may be differentiated from meningococcal meningitis by means of a bacteriological examination of the cerebrospinal fluid; moreover, in pneumococcal meningitis the causative agent may sometimes be found bacterioscopically in stained smears of the cerebrospinal fluid.

Pneumococcal meningitis is most commonly the result of a septicemic process which complicates the course of pneumonia, suppurative otitis, mastoiditis or cerebral abscess.

Development of pneumococcal meningitis is favoured by overcooling of the organism, owing to which this disease is usually observed during the cold time of the year. In the presence of a purulent focus in the organism the role provoking the development of pneumococcal meningitis may be played by various head injuries or by pneumococcal infection which successively affects the meninges injured prior to the infection. The disease affects predominantly children.

A certain role in the pathogenesis of the disease is played by other preceding diseases (for example, rickets), avitaminoses and nutritional disorders.

The clinical picture of the disease is characterized mainly by an acute onset; after moderate chills the temperature rises in the course of several hours to 39-40°C. A gradual onset of the disease is possible only in 20-25 per cent of infants.

A characteristic pose—overextended head and flexed legs and thighs—is observed in all patients from the very first hours of the disease. The meningeal phenomena are manifested in rigidity of the occipital muscles, positive Kernig's sign and Brudzinski's neck and symphysis signs; children additionally exhibit a tenseness and bulging of the great fontanel. In some cases pathologic symptoms on the part of cranial nerves are noted (paralyses of the 7th or 3rd and 4th pairs). Hemipareses and symptoms of purulent meningoencephalitis are possible.

The temperature curve is either of a constant or hectic type, long subfebrility being much more rarely observed from the very beginning of the disease. Muscular spasms and often repeated vomiting may occur all through the febrile period of the disease.

The patients' blood exhibits neutrophilic leucocytosis (up to 20,000-25,000 leucocytes per 1 mm³) with a sharp shift to the left, all the way to myelocytes; the ESR is considerably accelerated. The cerebrospinal fluid flows out under elevated pressure; it is pussy, frequently greenish, and contains clots of fibrin.

In half the number of cases the protein in the cerebrospinal fluid is elevated to 1.5-5 per cent, while in other cases it may not exceed the norm. Pandy's and Nonne-Apelt's tests are sharply positive. During the first hours of the disease, before treatment with antibiotics, the cerebrospinal fluid contains pneumococci which are found by bacteriological and bacterioscopic examinations.

The cerebrospinal fluid is marked by greatly elevated cytosis (up to 800-1,000 cells per 1 cu mm) increased mainly by neutrophils. If the cerebrospinal fluid contains any pneumococci, Gram stained smears show them mainly outside leucocytes and but partly phagocytosed by polymorphonuclear leucocytes.

The disease is diagnosed on the basis of the clinical picture, anamnesis, laboratory blood test (haemogram) and cerebrospinal fluid. The prognosis is usually serious. Treatment—penicillin.

In *purulent Pfeiffer's meningitis* the onset is acute with chills and a rapid rise in temperature, which is followed by symptoms of meningoencephalitis, and in children also by dyspepsia. The patient is in a grave general condition: extreme toxicosis, adynamia, motor unrest, repeated vomiting and meningeal phenomena (Kernig's and Brudzinski's signs, and rigidity of occipital muscles).

Focal affections of the central nervous system are characteristic, particularly frequently with development of pareses of the 3rd, 4th and 7th pairs of cranial nerves.

In some cases motor disorders, protracted loss of consciousness and encephalitic symptoms are observed; stable hemipareses are possible.

The cerebrospinal fluid is pussy, noted for neutrophilic pleocytosis, elevated protein (0.99-33%), positive Pandy's test and 30-60 mg% of sugar. Microscopy of Gram-stained smears of the cerebrospinal fluid (mainly from the precipitate of centrifuged fluid) reveals Afanasyev-Pfeiffer's bacilli; bacteriological examination of the cerebrospinal fluid is more reliable, but it must be remembered that under the influence of antibiotic therapy the causative agent soon ceases to be discovered.

The blood is characterized by leucocytosis (up to 15,000-25,000 leucocytes per 1 cu mm), sharp neutrophil shift to the left (all the way to myelocytes) and aneosinophilia. Treatment—levomycetin.

In some cases epidemic meningitis must be differentiated from severe forms of typhus, seasonal encephalitides, croupous pneumonia and poliomyelitis.

Treatment. All patients must be hospitalized (in special wards or isolators and compartments).

The patients need watching and thorough care, including swabbing of the oral cavity, prevention of bedsores and systematic evacuation of the bowels.

The patients must be prescribed a diet of semiliquid, easily assimilable, high-caloric foods containing plenty of vitamins C and B₁.

The most effective therapeutic agent is penicillin which is administered intramuscularly; adults are given 900,000-1,500,000 U per day divided into 2-3 equal injections, the antibiotic dissolved in a 0.25 per cent novocain solution.

The patients are simultaneously prescribed 1 g of norsulphazol or sulphadimezin (sulphamezathine) 4 times per day.

During the first 4 days of treatment, in addition to the intramuscular injections, patients are administered once a day into the vertebral canal a sodium salt of crystalline penicillin (60,000-100,000 U for adults, and according to age for children) dissolved in 6 ml of physiologic solution, 8-10 ml of cerebrospinal fluid being withdrawn from the vertebral canal before this administration. *Only sodium salt* of penicillin must be used for these injections which are discontinued as soon as the cerebrospinal fluid is characterized by pleocytosis (up to 100 cells).

Endolumbar administration of penicillin may be relinquished, and the antibiotic may be administered only intramuscularly in massive doses (1,800,000 U 6 times per day for 5-7 days).

The duration of the course of penicillin injections is determined not only by the disappearance of the clinical signs of the disease, but also by the results of repeated examinations of the cerebrospinal fluid (disappearance of the pussy character of the fluid, decrease in the protein and the leucocytes to normal, and absence of meningococci).

Patients may be discharged from hospital after disappearance of the clinical signs of the disease, normalization of the cerebrospinal fluid, and absence of meningococci in the smears of mucus from the fauces of the patients (in two bacteriological examinations). Moreover, it is necessary to keep strictly to the schedules of isolation (no discharge before 30 days have elapsed since the beginning of the disease).

Prevention. Epidemic meningitis may be prevented by revelation and isolation of patients, rational therapy, and revealment

of bacteria carriers (especially in closed children's institutions) by examination of all the children and attending personnel.

Carriers of the infection (children and adults) must not be admitted to nurseries, kindergartens and other children's institutions.

Normal, uninjured mucous membranes of the nasopharynx and fauces prevent the penetration of meningococci into the organism on contact with carriers of the infection. Sanitation of the nasopharynx is therefore an important means of preventing epidemic meningitis.

In children's institutions quarantine must be established on the 7th day after discovery and hospitalization of a patient. It is necessary to carry out a careful disinfection of all premises as it is done in cases of all other air-borne infections.

MUMPS (EPIDEMIC PAROTITIS)

Aetiology. The disease is caused by a filtrable virus (*Pneumophilus parotitidis*) which has been obtained in pure culture. The source of infection is a mumps patient.

Epidemiology. Epidemic parotitis is an air-borne infection. The disease usually affects children, although cases of it and even epidemics of this disease may occur among adults. The incidence of the disease rises during the cold time of the year (especially from January to March). There is a passive virus carrying: convalescents continue to be contagious for 14 days after disappearance of the clinical symptoms.

Incubation period. The incubation period is 14-21 days. In rare cases the incubation may last 30 days.

Clinical picture. All the main symptoms are associated with the affection of the parotid gland by the filtrable virus. The disease sets in with a short prodromal period (general indisposition, headache, loss of appetite) after which the temperature rises to 38.5-39.5°C and one of the parotid glands enlarges. The swelling of the parotid gland becomes well visible in front of the ear and subsequently behind and below the ear (below the angle of the lower jaw). The earlobe sticks somewhat out (Fig. 102), while the fossa behind it fills out. Palpation of the gland is slightly painful. The patient feels a certain tenseness in the region of the gland and pain during talking and chewing. Affection of both parotid glands lends the face a pearshaped appearance.

The swelling of the parotid gland is followed by cessation of secretion of saliva on the affected side (secretion of saliva is restored only on the 5th day of the disease). After 1-2 days of the disease similar phenomena may occur on the other side.

In typical cases with affection of one parotid gland the febrile period is 3-4 days and only in more severe cases it may last 6-7 days.

In adults the disease runs a much severer course than in children.

After the febrile period the parotid glands quite rapidly return to normal size. The most frequent complication of the disease in adults is orchitis, which is accompanied by intense pains in the affected testis and a considerable rise in temperature. In boys orchitis occurs less frequently. Affection of the pancreas is possible.



Fig. 102. Mumps (epidemic parotitis) patient with affection of the right parotid gland

Compression of the facial nerve by the enlarged parotid gland may lead to its paresis which, however, passes quite soon even without any therapeutic intervention (after diminution in the swelling).

Meningeal and meningoencephalitic forms of the disease are observed quite infrequently. An attack of the disease confers lasting immunity.

Diagnosis. The disease is diagnosed on the basis of epidemiological data (contact with a patient) and the clinical picture. The complement fixation test may be used for laboratory diagnosis.

Differential diagnosis. In differentiating the disease from phlegmonous parotitis it should be remembered that mumps patients have leucopenia, relative lymphocytosis and monocytosis. In phlegmonous parotitis the tissue of the gland softens.

Treatment. The patients must be isolated at home and kept in bed. Semialcohol hot compresses must be applied to the affected gland, and as soon as the swelling begins to abate a gauze dressing with a heavy layer of cotton is applied to the same area.

In view of the disturbed secretion of saliva and for the purpose of preventing secondary infection the oral cavity must be frequently gargled with a 2 per cent boric acid solution and a 1 : 1,000 rivanol (2-ethoxy-6,9-diaminoacridine lactate) solution. In cases of small children the mouth must be swabbed with a cotton tampon soaked in one of these disinfectants.

Prevention. Patients must be isolated until the 21st day of the disease. A quarantine must be established in children's institutions.

The methods of producing cultures of the filtrable virus --causative agent--which have now been elaborated make specific (inoculative) prevention of the disease possible.

INTEGUMENTARY INFECTIONS

The infectious diseases which develop as a result of penetration of the causative agent through injured skin and mucous membranes form a special group of diseases.

Infection with erysipelas and tetanus occurs in this manner. The skin, mucous membranes and soft tissues may become damaged as a result of everyday-life, industrial, agricultural and other injuries.

These infectious diseases are often called traumatic infections. As a rule, they are caused by various pathogenic bacteria.

ERYSIPELAS

Erysipelas is a general acute infectious disease characterized by a sudden onset, fever and, in the region of the atrium of infection, a peculiar inflammation of the skin and mucous membranes sharply demarcated from the surrounding unaffected tissue.

Actiology. The disease is caused mainly by haemolytic streptococci which are widely distributed in nature. Sometimes the disease is caused by staphylococci.

Pathogenesis and pathologic anatomy. Streptococci may invade the skin through various skin injuries, for example, through scratches, abrasions and excoriations, and as a result of contamination of wounds. However, invasion of streptococci is alone not enough to develop erysipelas; this disease can develop only in cases of certain susceptibility of the organism, its peculiar reaction.

From the atrium of infection the streptococci spread in the skin along lymphatic spaces and capillaries where they intensively multiply. Owing to the increased permeability of the blood capillaries of the skin the tissues become impregnated with serum and the patient develops hyperaemia, oedema and infiltration of the skin in the focus of affection.

The general symptoms of erysipelas (elevated temperature, headache, vomiting during the first hours, tachycardia) are due to

intoxication of the organism resulting from absorption of toxic substances formed by the destruction of the microbes and disintegration of tissues; bacteriaemia may also develop.

The erysipelatous process may also develop on the mucous membranes, for example, of the fauces and nose.

In addition to the most typical erythematous inflammation erysipelas sometimes involves formation of blisters and phlegmons; it may also occur in other clinical forms.

An attack of the disease sensitizes the organism, and in some cases the disease may recur, often with the same localization of the process.

Epidemiology. Infection with erysipelas is quite possible in cases where the skin has abrasions, excoriations, bruises and scratches, or is otherwise inadequately cared for, especially since the causative agent of the disease is widely distributed in nature. At the same time people are far from equally susceptible to erysipelas, and for its development the disease therefore requires not only penetration of the streptococcus into the organism through injured skin, but also a certain susceptibility of the organism. The incidence of erysipelas is higher during the cold time of the year.

Erysipelas may occur not only as a separate disease entity, but also as a traumatic infection due to injury of soft tissues. Sometimes it occurs as a secondary infection due to a microtrauma of the skin and mucous membranes and develops as a result of a sensitization of the organism or lowering of its general resistance caused by some general infectious disease.

Clinical picture. The incubation period varies from several hours to 3-5 days.

As a rule, the disease sets in acutely with chills and a rapid rise in temperature to 39-40 C and higher. The first hours of severe cases of the disease are often accompanied by very intense chills and, owing to the extreme general intoxication, by vomiting and sometimes by loss of consciousness and delirium. At the present time, however, such very severe cases are rare.

In cases of *moderate severity* the pulse becomes faster in keeping with the rise in temperature. The changes in the pathologic focus in cases of erythematous erysipelas develop as follows. A small, but rapidly enlarging red macule appears at the atrium of infection. The affected part of the skin is painful and, along the periphery, elevated above the surrounding skin. The skin is hot and, stretched by tissue exudate, is lustrous all over this area. Along the edges the affected area is circumscribed by a serrated, scalloped line which sharply separates it from the unaffected skin. Along the borders of the erythematous area there is an inflammatory elevation (infiltrate) which is very painful to touch. It is characteristic that during the subsequent course of the disease the affected area enlarges at different rates in different patients. The intense hyperaemia and

fanciful contours of the affected part of the skin make it look like tongues of flame (Fig. 103).

Erythematous erysipelas most commonly affects the skin of the face and head; its second most frequent localization is on the lower extremities, and the third—on the upper extremities. Easily injured parts of the skin—in the region of the external meatus, at the corners of the mouth and at the nostrils—serve as the atrium of infection in cases of erysipelas of the face and head. Erysipelas may spread from the skin to the mucous membranes and vice versa.

Sometimes the erysipelatos process may affect extensive areas of the skin (*wandering erysipelas*), but upon reaching natural folds of the skin the inflammatory phenomena usually spread no further.

In cases where several vesicles or blisters filled with serous fluid have formed on the part of the skin affected with erysipelas the disease is called *erysipelas bullosum*. Since the blisters sometimes open spontaneously, failure to observe the rules of asepsis may lead to penetration of secondary purulent infection through the newly-formed atrium of infection.

The spread of streptococci from the upper layers of the skin to the lymphatics and blood vessels of subcutaneous tissue results in development of phlegmons. Compression of the soft tissues by the transudate may give rise to necrosis—*gangrenous erysipelas*.

The temperature curve in erysipelas varies, but is most frequently of a remittent type; the type of temperature curve is substantially influenced by antibiotic therapy (Fig. 104).

The general phenomena in erysipelas consist in a violent, but brief temperature reaction, headache, general weakness and jadedness and, only in cases of extreme intoxication, in clouded consciousness. Excitement and delirium are possible.

With the beginning of recovery the patient's general condition noticeably improves, the temperature drops, and the appetite and sleep are restored. In the affected area of the skin hyperaemia disappears, oedema diminishes, and the skin begins to scale.

Relapses are observed in about 7-8 per cent of the people who have survived erysipelas; the relapses occur at different periods of time after the primary attack of the disease, usually with the same localization.

Reinfection with erysipelas due to sensitization of the organism to the streptococci which cause this disease is possible. There have been cases where erysipelas recurred in the same person over a period of 5-7 years.

Complications. As a result of permanent lymph circulation disorders (especially in the lower extremities) in erysipelas *elephantiasis* may develop.

~~and~~ In addition to the afore-mentioned complications some patients develop subcutaneous abscesses, secondary septic pneumoniae and diffuse nephritides; if the defensive factors of the organism are

particularly weakened by debilitating diseases, streptococcal sepsis develops.

If erysipelas is localized on the face, the inflammatory process may spread to the cellular tissue of the orbit, which may lead to neuritis of the optic nerve and thromboses in the cranial cavity.

As was already noted, erysipelas may also affect mucous membranes. If it spreads to the nasal mucosa, the patient develops an abundant purulent discharge from the nose. The spread of erysipelas to the faucial mucosa is accompanied by high temperature, violent pains during swallowing, intense hyperaemia and oedema of the tonsils and palatine arches. A parturient woman may develop erysipelas of the parturient canal in cases of birth trauma.

Development of erysipelas on mucous membranes is characterized by the same signs (hyperaemia, rapid spread of the process) as in affection of the skin.

Erysipelas does not confer stable immunity; relapses and recurrent cases are observed; the latter are due to reinfection with streptococci.

Diagnosis. Typical cases of erysipelas are not difficult to diagnose. The characteristic inflammatory process on the skin accompanied by symptoms of general intoxication and a rise in temperature, sharp demarcation of the inflamed area from the surrounding skin and the presence of a very painful inflammatory elevation along its periphery make it possible to establish a correct diagnosis of erysipelas.

Differential diagnosis. In cases accompanied by considerable oedema of the soft tissues it is necessary to differentiate the disease from a phlegmon. In the latter the hyperaemic zone gradually blends with the unaffected surrounding tissue and the pain is noted mainly in the centre of the affected area.

Prognosis. In typical cases of erysipelas of moderate severity the prognosis is usually favourable and with timely and vigorous treatment the patients recover. However, relapses and various complications, including elephantiasis, are not excluded. The complications always render the prognosis more serious.

In patients suffering from nutritional disorders and avitaminoses, in elderly people and in cases of chronic intoxications and a number of concurrent chronic diseases of the skin erysipelas runs a protracted and severe course.

Treatment. All erysipelas patients must be hospitalized.

It is important to keep the patient's skin clean and to see to it that the bladder is emptied regularly. The patients must be prescribed a semiliquid dairy and vegetable diet, and plenty to drink; the diet must be enriched with vitamins, especially ascorbic acid.

Observance of the rules of hygiene and asepsis, as well as thorough care of the patients, are particularly necessary in cases of erysipelas bullosum and gangrenous erysipelas, and in cases accom-

panied by purulent complications, for example, abscesses in subcutaneous tissue, etc. The dressings removed from patients must be burned.

The main agent in the treatment of erysipelas is penicillin. Already on the second day of treatment with this antibiotic the patient's condition considerably improves, the intoxication disappears, the temperature begins to fall, the focus of skin affection ceases to enlarge, and the patient finally completely recovers. Penicillin is administered intramuscularly in a dose of 600,000-900,000 U per day for 5-6 days. In severe cases the dose of penicillin must be increased to 1,000,000-1,200,000 U per day and the course of treatment must be prolonged.

Good results are produced by combined treatment with penicillin and levomycetin; the latter is administered per os in a dose of 0.5 g 4 times per day. Tetracycline is also quite effective.

If recovery is slow, the patient must be given, in addition to penicillin, transfusions of the same group or 1(0) group of blood in a dose of 150 ml every 2-3 days. To desensitize the organism and prevent relapses, dimedrol (in a dose of 0.05 g 3 times per day) or diazoline (5-benzyl-1, 2, 3, 4-tetrahydro-2-methyl-SH-pyridine-indole) is administered.

If no injections can be made, levomycetin is administered in a dose of 0.5 g 6 times per day for 5-6 days, but this treatment is less effective than that with penicillin or with penicillin combined with levomycetin; the temperature falls later and the local pathologic disturbances are eliminated more slowly.

Streptocide (1 g 4 times per day for 5-6 days) or norsulphazol are rarely used in the treatment of erysipelas today, since treatment with these drugs is less effective than that with penicillin or levomycetin.

Chemotherapy is supplemented by ultraviolet irradiation of the affected areas of the skin (several 10-minute sessions of irradiation at a distance of 100 cm from the mercury quartz lamp). During irradiation the patient's eyes must be protected with dark glasses.

In cases of erysipelatous affection of the eyelids it is necessary to wash the eyes daily with a 2 per cent boric acid solution and to instill a 2 per cent protargol solution 3-4 times per day. Development of gangrene or a phlegmon requires surgical intervention and an increased dose of penicillin combined with streptomycin.

Prevention. It is necessary to keep the skin clean and intact (preventing abrasions, cracks and excoriations, especially on the feet) and avoid scratching or bruising the face and nasal mucosa because the subungual spaces often contain streptococci.

Primary treatment of wounds serves as a reliable means of preventing erysipelas as a traumatic infection.

In making exploratory punctures (for example, in the pleural cavity) or infusions of drugs (subcutaneously, intramuscularly or

intravenously) it is necessary to observe strict asepsis to prevent introduction of streptococcal infection into the skin or mucous membranes with possible development of erysipelas.

To prevent reinfection with erysipelas, all persons who have survived an attack of the disease must strictly observe the rules of personal hygiene and avoid overcooling.

TETANUS

(*Tetanus* is a human traumatic infection resulting from penetration of the spores of the *Bacillus tetani* into the wounded surface of soft tissues with liberation, by the formed vegetative (bacillary) forms of these bacteria, of a very strong exotoxin which affects the central nervous system. The disease is accompanied by tonic spasms of voluntary muscles and exaggerated reflex activity.

Aetiology. The vegetative form of the causative agent of tetanus is a thin motile rod about 1.2 μ long and 0.6-0.7 μ thick. In the external environment the bacillus forms at one of its ends a spore resembling a drumstick. The spores are very stable against heat and antiseptics.

The tetanus bacilli are gram-positive and are readily cultivated under anaerobic conditions. Upon gaining entrance into crushed and necrotic human tissues deprived of normal oxygen supply the spores of the *B. tetani* develop into their vegetative (bacillary) form.

The *B. tetani* produce an extraordinarily strong exotoxin which affects the central nervous system of man and certain animals which are sensitive to it.

The intestines of man and animals often contain *B. tetani* which are eliminated in the faeces; that is why the soil, especially when considerably contaminated with faeces of man and animals, may contain a great number of spores of *B. tetani*.

Wounds contaminated with the soil of populated areas are particularly dangerous.

Epidemiology. Tetanus is most commonly observed in people whose work may lead to contamination of wounds with earth. These people may become infected when the soil comes in contact with even the most superficial injuries of the skin and mucous membranes.

Pathogenesis. The exotoxin produced by *B. tetani* spreads from the atrium of infection along nerve trunks (perineurally) to the spinal cord and causes a functional increase in its reflex excitability and a number of pathologic structural changes in the nerve cells of the grey matter of the spinal cord. In addition to the main route of spreading from the atrium of infection along the nerve trunks, the toxin may also spread all through the organism with the blood, thereby likewise causing toxic affection of the nerve cells in the spinal cord and brain.

The tetanus toxin stimulates the motor centres of the brain and the cells of the anterior horns of the spinal cord. The main symptoms of the disease develop as a result of the action of the tetanus toxin on the various parts of the central nervous system and manifest themselves as protracted tonic spasms of the skeletal muscles and their exaggerated reflex activity.

Incubation period. The average incubation period is 6-14 days but it may be from 1 day to 2 months. In individual cases, very rare to be sure, the incubation period of tetanus may be prolonged to several months.

Clinical picture. The following forms of the disease are distinguished: (a) according to severity—mild, moderately severe and severe; (b) according to the course—fulminating, acute, subacute, relapsing and chronic tetanus; and (c) according to the extent of its spread—localized and generalized tetanus.

The earliest sign of tetanus is the appearance of dull, gnawing pains at the atrium of infection where the wound has already completely healed.

As early as the end of incubation, 1-2 days before the appearance of *trismus* (as one of the most reliable and earliest signs of tetanus), it is possible to evoke the reflex of the muscles of mastication by asking the patient to half-open his mouth and carefully tapping with the forefinger on the face above the location of the masseter muscles; the result is a tonic spasm of these muscles. An analogous reflex may be evoked by putting a spatula on the patient's lower teeth, while the patient's mouth is half-open, and, by holding the spatula with one hand, tap on it with a finger of the other hand.

The early signs of tetanus also include rigidity and tonic spasms of muscles in the area of injury on the extremities; by grasping the extremity with both hands near the site of injury and quickly kneading the muscles (as in massage) it is possible to feel the appearance of marked local rigidity. True, this sign is observed only in 40-45 per cent of the cases.

The patient soon develops trismus—tonic spasm of the muscles of mastication and involuntary locking of the jaws. The patient's face assumes a sardonic expression (*risus sardonicus*) due to the tonic spasm of the muscles of facial expression (knitted brow). Moreover, the patient's face expresses horror, the head is thrown back, the teeth are clenched and the vessels of the sclerae are filled with blood. The skin of the trunk is often moist because of excess perspiration.

Gradually, in the course of a few hours, one group of muscles after another develops spasms in a very definite succession—*descending tetanus*. The abdominal muscles grow very tense, and the anterior abdominal wall becomes hard as a board. The long extensor muscles of the back are particularly strongly contracted, and at the time of convulsions the patient's body is arched, the patient

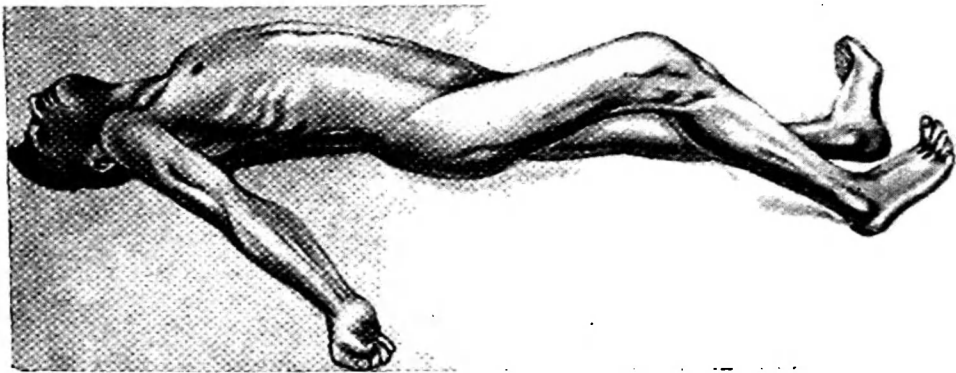


Fig. 105. Tetanus patient (opisthotonos)

resting in bed only on the back of his head and the heels (*opisthotonos*, Fig. 105). The head is often thrown back. Owing to the spasms it is difficult or even impossible to swallow food and liquid, the urine and stool are often retained. The tonic spasms are much less intense in the muscles of the extremities; the muscles of the hands, fingers and feet are usually unaffected. Tonic spasms of the intercostal muscles are sometimes observed; a strong contraction of the abdominal muscles may give rise to flexion of the body (*emprosthotonos*). It is characteristic that the patients perspire excessively.

The temperature often persists at high figures, but is not regular. The disease lasts a total of from 10 to 30-35 days. Gradually the attacks grow less frequent, and the patient's condition improves. Sometimes the disease may become complicated with aspiration pneumonia.

Various courses of the disease. The foregoing was a description of the typical acute form of generalized tetanus.

Relapses of tetanus with renewal of the clinical picture of the disease in 1-2 months are very rarely observed.

In cases of *fulminating* tetanus the picture of the disease develops very acutely, and the patient may die during a severe attack of spasms with paralysis of the respiratory muscles.

In cases of *subacute* and *chronic* tetanus the disease lasts from 14-15 days to several months, but the attacks of spasms are observed less frequently and are not so tormenting; there are usually no general convulsions, and the rigidity of different groups of muscles increases gradually. These forms are most commonly the result of an atypical course of the disease in persons with partial immunity (for example, in cases of late administration of serum following an injury).

A peculiar variety of tetanus is so-called *localized tetanus* in which spasms affect only the muscles of the face or other groups of muscles.

Sometimes tetanus develops in women after criminal abortions and in newborn children if the rules of asepsis are violated when tying the cord; in these cases the incubation period is short and the prognosis very serious. Tetanus may develop after burns and frost bite, as well as after postpartum and postinjectional diseases.



Fig. 106. Cephalic tetanus (paralysis of the left facial nerve)

It is difficult to diagnose *mild forms* of tetanus in which the tonic spasms of muscles are limited to moderate symptoms of trismus and later spread only to the muscles of facial expression and of the back of the head without generalized convulsions (Fig. 106).

The prognosis is always serious, especially in cases with a short incubation period, as in head injuries.

Diagnosis. Diagnosis of tetanus is based on anamnesis (contamination of a wound or damaged skin) and the clinical picture of the disease. The characteristic sequence of the development of all symptoms of the disease must be taken into account.

Differential diagnosis. In typical cases the diagnosis is so simple that it requires no differential diagnosis. But atypical cases often present great difficulties. Despite the certain similarity to *strychnine poisoning*, tetanus is characterized by descending muscular spasms and normal pupils, whereas in strychnine poisoning the spasms begin in the lower extremities and ascend, while the pupils

are considerably dilated. It must be emphasized that in tetanus during the intervals between the attacks of spasm the muscles do not relax (they remain in a state of tonic contraction), whereas in strychnine poisoning they do relax.

In some cases tetanus must be differentiated from *rabies* (see chapter on rabies), epilepsy and severe attacks of hysteria; the question of diagnosis is decided on the basis of the sum total of data; a state of eclampsia must be taken into consideration.

Treatment and care. The success of the treatment of tetanus patients is determined primarily by earliest possible and repeated administration of an adequate dose of antitetanic serum (tetanus antitoxin). The dose must be chosen in accordance not only with the severity and period of the disease, but also with the massiveness of the infection. The first injection is the most effective.

During the first day *tetanus antitoxin* is administered intramuscularly in doses of 100,000-350,000 U (the first administration is made by the method of preliminary desensitization—see page 78). In severe cases of tetanus antitoxin is simultaneously administered into the vertebral canal (about 30,000-50,000 U) after first withdrawing 5-6 ml of cerebrospinal fluid; the antitoxin is administered slowly. However, many authors deny, not without reason, the benefits of intralumbar administration of the antitoxin. The antitoxin should be administered intramuscularly for 3-4-5 days until a sufficiently stable clinical effect is produced. The daily doses of antitoxin administered on the 2nd, 3rd and subsequent days may be 100,000-125,000 U. On the 1st and 5th days of treatment 1.5 ml of tetanus antitoxin is administered subcutaneously.

To decrease the spasms of the muscles, the patient must be given chloral hydrate in an enema (1.5 g or chloral hydrate per 100 ml of starch water in a small enema) after a preliminary cleansing enema.

The spasms also decrease after intramuscular administration of a 10 per cent magnesium sulphate solution (40-50 ml per day). In cases of particularly intense motor excitement it is necessary to inject morphine and pantopon. In severe cases the patients are administered a tracheotomy and are given artificial respiration by means of an iron lung; at the same time they are prescribed curarimimetic substances (for example, diplacin) and aminazine (chlorpromazine).

Patients must be placed in separate well-ventilated wards. It is necessary to exclude the least possible shaking of the bed and all other irritations (noise, movement of air currents). In severe cases, if the patients cannot feed themselves, they must be fed by the personnel. The patients must be fed when they have no spasms in order to prevent aspiration of food or drink. If a patient cannot be fed normally, it is necessary to feed him through a tube (see Fig. 10) or through nutrient enemas.

In severe cases it is necessary to place rubber rings under patients in order to prevent bedsores.

The wound which served as the atrium of infection must be treated according to the rules of surgery (excision of the wound following the injury).

To prevent pneumonia which is often a complication of tetanus and the cause of death, patients must be administered intramuscularly 300,000 U of penicillin 4 times per day. To prevent spasms, pneumonia and asphyxia, curarimimetic substances may be used; these substances—diplacin, condelifin, etc.—paralyse the respiratory muscles, eliminate muscular spasm (by blocking of the neuromuscular junction and preventing response to nerve impulses) and prevent development of asphyxia and pneumonia. If these drugs are used, it is necessary to ensure external respiration by means of special respiratory apparatus (see Fig. 97); the patients must be additionally administered aminazine and small doses of luminal and caffeine.

Prevention. In all cases it is necessary to prevent contamination of wounds and abrasions on the skin. In cases of injuries, the patient must be given immediate primary surgical treatment. Simultaneously 2,000-3,000 U of tetanus antitoxin must be administered subcutaneously (it is desirable that this should be done not later than 6-8 hours after the injury).

An important role in preventing tetanus among servicemen during the first and second world wars was played, in addition to the foregoing measures, by specific inoculations with tetanus anatoxin.

People who are continuously in danger of contaminating wounds with earth (navvies, miners) are now given inoculations with tetanus anatoxin: 1 ml is administered subcutaneously the first time and 1 ml again after 1 month and 2 months each.

The anatoxin used for inoculations is produced by treating the exotoxin of tetanus bacilli with formalin. The exotoxin loses its toxic properties and is transformed into an anatoxin which acts as a good antigen; in response to its administration the organism elaborates antitoxic immunity which prevents the development of tetanus.

The inoculations against tetanus may be combined with vaccination against typhoid fever and paratyphoids or against diphtheria and whooping cough by using a complex vaccine.

COMPLICATIONS OF DRUG THERAPY AND METHODS OF PREVENTING THEM

Antibiotics and sulpha drugs are obviously very effective agents for the treatment of infectious diseases. These agents have been very successfully used in the treatment of many infectious diseases, including so dangerous a disease as plague; the prospects of synthesiz-

ing new antibiotics or producing them from cultures of fungi are unlimited. However, the practice of treating infectious diseases has shown that in a number of cases, especially where massive doses of these agents have been used for a long time, the patients develop toxic and allergic manifestations which are the side effects produced by these agents and are known as complications of drug therapy. The most important symptoms of this pathologic condition, which often complicates antibiotic therapy, are toxic and allergic phenomena, and dysbacteriasis; in some cases it is difficult to draw a clear line between them in accordance with the mechanism of their development, although such symptoms as nausea and vomiting are of toxic origin, whereas urticarial eruptions on the skin and eosinophilia are allergic reactions.

"Drug disease" is an unhappy term because of the absence of a clearly defined symptom complex; it would be more appropriate to speak of complications of drug therapy, although the former term is very widely used.

The most important side effects of antibiotic therapy may be nausea, repeated vomiting, development of stomatitis and thrush, urticarial or roseolous eruptions on the skin, purpura, ecchymoses, dermatitis medicamentosa, hypotension, frequent liquid stool, elevated temperature, cyanosis of the lips, and dyspnoea. Sometimes eosinophilia is observed. The frequency and extent of these toxic and allergic phenomena or side effects produced by antibiotics, i.e., the symptoms of "drug disease", vary very widely; although some antibiotics have a good deal in common, there are also certain differences between them.

For example, treatment with biomycin or synthomycin produces complications more often than treatment with levomycetin, toxic and allergic manifestations, or side effects, produced by the latter appearing in 15-18 per cent of the cases.

Of the various manifestations, or side effects, produced by antibiotics special mention must be made of toxic suppression of the haematopoietic functions. People who are hypersensitive to levomycetin may develop phenomena of aplastic anaemia (in some cases even after taking small doses—only 5-6 g for a course of treatment).

Treatment with levomycetin and streptomycin sometimes gives rise to leucopenia and agranulocytosis. Treatment with penicillin increases blood-clotting and fosters formation of thrombi; some patients may develop eosinophilia or various dermatitides. Long external application of penicillin may give rise to severe exfoliative dermatitis and very often produces erythema and urticaria.

It should be remembered that nurses who continuously have to do with injections of streptomycin or penicillin may develop contact dermatitis (itching and stable erythema in the interdigital spaces; severer affections are accompanied by formation of erythematous patches, vesicles and subsequently crusts). To prevent contact derma-

titis, the medical personnel must wear rubber gloves, especially when many penicillin injections have to be administered.

Administration of some antibiotics sometimes produces urticarial eruptions, angioneurotic oedema and various manifestations of serum sickness, at times to the extent of severe anaphylactic shock.

These reactions may be *acute* (developing several hours after administration of an antibiotic) or *remote* (arising within 7-14 days); the reactions of the latter type are more typical of the side effects produced by penicillin.

In addition to urticarial eruptions, eruptions resembling exudative erythema or erythema nodosum may break out on the skin.

Dysbacteriasis produced in some patients by the action of antibiotics is sometimes accompanied by a considerable rise in temperature which may persist for several days. Such cases of drug disease make it necessary to differentiate them from various febrile diseases.

Antibiotic-resistant microbes (staphylococci, proteae, enterococci, pyocyanic bacilli, etc.) are capable of producing "superinfection" with development of staphylococcal pneumoniae, pseudomembranous colitis, etc.

In cases of biomycin treatment pseudomembranous colitis, eruptions of the type of polymorphous erythema, and eczematoid affections of the skin are sometimes observed.

Patients treated with streptomycin injections may develop erythematous, maculopapular and urticarial eruptions.

A rise in temperature is observed in some patients during the first 3 days of treatment with streptomycin; now and then aplastic anaemia may develop.

In some patients streptomycin affects the acoustic nerve and entire vestibular apparatus; such cases are often accompanied by disturbances in normal intestinal fermentation, suppression of the physiologic intestinal flora (dysbacteriasis) with a picture of diarrhoea, possible diffuse erythrodermas, urticarial eruption and fever.

Suppression of the normal flora in the oral cavity, intestines and reproductive system leads to dysbacteriasis with the result that the microbial flora which is antagonistic to pathogenic bacteria is no longer capable of playing its barrier role in the organism. Moreover, the vitamin balance in the organism is disturbed (metabolism of the vitamin B complex is particularly affected). In such cases staphylococci and yeasts often become pathogenic. The drug disease may result in affections of the colon (colitides), lungs (fungus pneumoniae) and other internal organs, and sometimes even in a generalized infection (moniliasis).

The patient's *individual sensitivity* to various drugs, the given antibiotic in particular, plays an important part in the development of the side effects.

As a rule, the side effects observed in some cases of antibiotic treatment are easily reversible. Stomatitides and thrush were also ob-

served before the introduction of antibiotics into therapeutic practice, especially in individual, greatly debilitated patients.

Antibiotic therapy most commonly produces side effects in persons affected with eczema, acute angioneurotic oedema and exudative diathesis. It is well known that, developing on the second or third day of antibiotic treatment, side effects may disappear without leaving a trace despite the continuing treatment, as is often observed in cases of prolonged administration of levomycetin, for example, in the 12-15-day course of uninterrupted treatment of typhoid fever patients. But side effects may be particularly strongly pronounced when large doses of antibiotics are used *without any system* and for *an unwarranted long time* or where patients are administered for *a long time massive doses* of two or more antibiotics. The patient's individual sensitivity to drugs combined with disorderly and long administration of massive doses of antibiotics to emaciated and extremely debilitated patients leads *in some cases* to severe generalized affection (moniliasis) caused by yeastlike pathogenic microorganisms *Candida albicans*. The signs of this severe, often septic condition of the organism are elevated temperature, intoxication, chills and sweat, tachycardia, and local affections of the oral mucosa, large intestine, kidneys, urinary tract, lungs, liver, and cardiovascular system. To prove that the sepsis is of a *Candida albicans* aetiology, it is very important, in addition to the foregoing clinical data, to examine microscopically the mucus from the oral cavity, the sputum and urine, which in positive cases reveal budding yeast cells and mycelium; in these cases allergic skin and serologic (agglutination and complement fixation) tests are positive. Moniliasis may end lothally. It should be emphasized that during treatment with antibiotics moniliasis occurs quite infrequently and only under the afore-mentioned conditions.

To prevent moniliasis during antibiotic treatment, it is advisable to give patients nystatin in pills (1 pill 4 times per day for 5-8 days).

Administration of "shock" doses of antibiotics is inexpedient because the rapid destruction of the causative agents of the infectious disease in the organism increases its intoxication due to the acute endotoxic reaction of aggravation with a possible development of collapse. In some cases a considerable overdosing of antibiotics, administration of "shock" doses and prolonged treatment with such doses may lead to severe affections of the haematopoietic system.

Prevention of side effects consists primarily in rational prescriptions of antibiotics really effective against the causative agent of the given disease. It is best to administer *medium* therapeutic doses and avoid administration for too long a time either of separate antibiotics or combinations of several antibiotics of a wide spectrum of action; it is necessary to check on the real results of the treatment without unnecessarily prolonging the therapeutic course.

With the synthesis and introduction into practice of antibiotics of a narrow spectrum of action the incidence of side effects will undoubtedly diminish. It is necessary to reveal in the patient's anamnesis cases of allergic reactions to antibiotic treatment and exercise caution, in prescribing appropriate drugs.

A certain role in preventing allergic manifestations during treatment with antibiotics is played by desensitizing therapy (transfusions of small portions of blood, diprozone [N-(2-dimethylamino-propyl) phenothiazine hydrochloride], diazoline [5-benzyl-1, 2, 3, 4-tetrahydro-2-methyl-SH-pyridine-indole] and calcium chloride). In some cases, because of the strongly pronounced phenomena of the "drug disease", it is necessary to discontinue the administration of antibiotics. Patients must be given adequate amounts of vitamins C, B₁ and B₂.

In cases of moniliasis it is necessary immediately to discontinue administration of all drugs and antibiotics, widely administer symptomatic treatment, and support the cardiovascular function and respiration; administration of special drugs, which suppress the growth of the *Candida albicans type of fungi*, and of a special vaccine (prepared from appropriate strains of these fungi) for purposes of immunization (a total of 6 injections, administered every other day) is now suggested.

To treat the "drug disease" developing in the form of generalized moniliasis, it is recommended to administer nystatin per os (2 pills 4 times per day for 8-10 days).

Treatment with iodine preparations is less effective. Mycostatin is administered the same as nystatin.

Treatment with sulpha drugs may become complicated by persistent vomiting, skin eruptions, dermatitides, and crystalluria in the urinary tract (pains in the small of the back, oliguria, and erythrocytes in the urine) developing as a result of precipitation of sulpha drugs in the kidney tubules and their blocking. Upon the appearance of symptoms of crystalluria it is necessary immediately to discontinue administration of sulpha drugs and give the patients plenty of mineral water to drink; in cases of severe oliguria or anuria catheterization of the ureters has to be resorted to.

To prevent crystalluria, patients treated with sulpha drugs must be given plenty to drink. There is less chance that the patients will vomit if they drink down every dose of the drug with a 3 per cent solution of bicarbonate of soda.

Treatment with sulpha drugs may involve one of the three following categories of side effects.

The first category of complications of sulpha drug therapy (mild forms) includes elevated temperature, dermatitis (with erythema, morbilliform, urticarial and nodular eruptions), nausea and micro-crystalluria. The blood exhibits hyperleucocytosis with a sharp shift

of the leucocyte formula to the left. In such cases administration of sulpha drugs must be immediately discontinued.

The second category of complications (moderately severe forms) is characterized, in addition to the foregoing symptoms, by toxic hepatitis, renal colic and neuritides of peripheral nerves. Leucopenia is typical of the blood picture.

The third category of complications (severe forms) is marked by muscular spasms, acute haemolytic anaemia, symptomatic thrombopenic purpura (up to 30,000-35,000 thrombocytes per 1 cu mm of blood), agranulocytosis (up to 650 leucocytes per 1 cu mm of blood with 90-95 per cent lymphocytes). In cases accompanied by complications of the second and third categories sulpha drug treatment must be immediately discontinued and the patients must be given plenty of alkaline mineral water to drink, and massive subcutaneous infusions of physiologic solution and 5 per cent glucose solution (preferably by the drip method); cases of anuria require catheterization of the ureters.

The frequency and extent of all afore-mentioned side effects are largely determined by the individual sensitivity of the patient's organism to sulpha drugs.

Supplements

Incubation Periods of Various Infectious Diseases

Disease	Incubation period			Note
	Average	Minimum	Maximum	
Botulism	12 hours	1-2 hours	26 hours	
Typhoid fever	15 days	7 days	21-23 days	
Dysentery	3 days	2 days	7 days	
Paratyphoid A	8 days	2 days	14 days	
Paratyphoid B	6 days	3 days	15 days	
Food poisoning	6 hours	2-3 hours	24 hours	
Typhus	14 days	6 days	21 days	
Relapsing fever (louse-borne)	7-8 days	2 days	14 days	
Relapsing fever (tick-borne)	7 days	5 days	10 days	
Leishmaniasis	21 days	10 days	9 months	
Pappataci fever	5 days	3 days	8 days	
Malaria	12 days	6 days	31 days	In tertian malaria sometimes 7-9 months
Seasonal encephalitis:				
tick-borne	14 days	8 days	23 days	
Japanese	14 days	4-7 days	21 days	
Chickenpox	14 days	10 days	21 days	
Influenza	2 days	Several hours	3 days	
Diphtheria	5 days	2 days	10 days	
Whooping cough	9 days	2 days	15 days	
Measles	10 days	6 days	18 days	In patients immunized with antimeasles serum 28 days
Smallpox	10 days	5 days	15 days	
Poliomyelitis	7 days	3 days	10 days	
Scarlet fever	3-6 days	Several hours	11 days	

(Continued)

Disease	Incubation period			Note
	Average	Minimum	Maximum	
Epidemic meningitis	2-3 days	4 days	7 days	Rarely up to 1 year
Epidemic parotitis	18 days	3 days	30 days	
Rabies	40 days	15 days	80 days	
Brucellosis	14 days	7 days	8 weeks	
Leptospiroses	7 days	3-4 days	20 days	
Glanders	7 days	3 days	14 days	
Anthrax	3 days	Several hours	8 days	In persons who were vaccinated or administered se- rum — up to 12 days
Tularaemia	8 days	1 day	21 days	
Plague	3-4 days	Several hours	9-10 days	
Foot and mouth disease	4 days	2 days	6 days	Sometimes up to 1 year and longer (in opera- tions for re- moving splin- ters)
Erysipelas	20 hours	3 days	6 days	
Tetanus	7-10 days	1 day	36 days	

Supplement 2

Methods of Taking Material for Laboratory Examination

Disease	Material	Day of the disease	Time of laboratory reply	Note
Typhoid fever	1. Blood (10 ml from vein) in vial with 100-125 ml of bile or bile broth to obtain haemoculture	From the first day	In 4 days, preliminary in two days	Test must be repeated in 3-5 days
	2. Blood (2-3 ml from a vein or finger) in test-tube for agglutination test (at physician's assistant's station—3 drops of blood on a cellophane strip)	From the 8th or 9th day	Next day	
	3. Faeces (3-5 g) in special tube or sterile jar	From the beginning of the disease, but usually from the 2nd week	In 4 days, preliminary in 2 days	Must be mixed in the tube with equal volume of 30 per cent glycerin in physiologic solution
	4. Urine (50-100 ml) in sterile vial	Same	Same	
Paratyphoids A and B	1. Blood to obtain a haemoculture as in typhoid fever	From the 1st or 2nd day	As in typhoid fever	
	2. Blood for agglutination test as in typhoid fever	From the 8th or 9th day		
	3. Faeces and urine as in typhoid fever			

(Continued)

Disease	Material	Day of the disease	Time of laboratory reply	Note
Dysentery	Faeces (3-5 g) in special tube or test-tube; mucosanguineous clumps must be chosen	From the 1st day	Same	Inoculation should be made, if possible, at patient's bedside
Food poisoning	1. Blood for haemoculture as in typhoid fever	Same	As in typhoid fever	
	2. Vomitus (15-20 ml) in special tube, or 150 ml in jar	Immediately	Same	
	3. Faeces (3-5g) in special tube or jar	From the 1st day	Same	In glycerin mixture
	4. Blood for agglutination test	From the 8th or 9th day	Next day	
	5. Foodstuffs (remains of prepared food, remains of raw meat, tubular bones, fish)	From the 1st day	In 4 days	
Asiatic cholera	1. Vomitus in special tube or in well-closed sterile test-tube	Same	Preliminary in 12 hours, final in 24-36 hours	Material must be carefully packed and sealed
	2. Faeces (3-5 g) in special tube or well-closed sterile test-tube	Same		
	3. Two smears of faeces on slides	Same	Same day	
Typhus	Blood (2-3 ml from vein or finger) for agglutination test with <i>Rickettsia prowazeki</i> or for the Weil-Felix test	From the 5th to 7th days	Next day	If a low titre is obtained the test must be repeated in 3-5 days

Relapsing fever	Blood from finger as 2 smears and 2 thick drops on slides	During attack	Same day	Blood must be taken only at high temperature
Malaria	Same	Same	Same	
Diphtheria	Membrane or mucus from fauces and nose on a sterile cotton tampon in plugged sterile test-tube	From the 1st day	Next day	Tampons must be sent to laboratory immediately. They must be guarded against cooling
Epidemic meningitis	Cerebrospinal fluid (5-10 ml obtained by puncture) in sterile test-tube	Same	Same	
Brucellosis	1. Blood from vein for haemoculture; inoculation of 5 ml in each of 2 bottles containing a special medium (broth) 2. Blood (2-3 ml from vein or finger) for Wright's agglutination test 3. Urine (10-20 ml) in sterile container for inoculation in laboratory	From the very onset of the disease From the 8th or 9th day From the first days	In 20-25 days Next day In 20-25 days	Inoculations of blood and urine may be made only in special laboratories

(Continued)

Disease	Material	Day of the disease	Time of laboratory reply	Note
Leptospiroses	1. Blood for haemoculture (2-3 ml from vein) inoculated in 10-12 ml of tap water or special liquid medium (see p. 280)	Same	In 8-10 days	Large number of leptospirae found in the liver, kidneys and adrenals of the animal
	2. Blood (5 ml) to infect guinea pig directly in the heart or abdominal cavity	Same	In 4-5 days	
	3. Blood (2-3 ml) for agglutination-lysis test	From the 5th to 7th days	Next day	
Glanders	1. Discharge from ulcers on sterile cotton tampon (for microscopy and inoculation)	From the first days	Same	Inoculations rarely yield positive results. Material is used for administration to male guinea pigs in which it produces specific orchitis (Straus' phenomenon)
	2. Mucus from the nose on sterile tampon	Same		
	3. Blood from vein (5-10 ml) in test-tube (during septicaemic stage of the disease)	Same		
	4. Sputum in special tube for inoculation and 2 smears on slides	Same		

	Next day		
Anthrax: (a) cutaneous form	Next day	Same	Contents of pustule and juice from ulcer taken with Pasteur pipette and smears on 2 slides stained with methylene blue for microscopy
(b) pulmonary form	Same	Same	Sputum in special sterile tube and 2 smears of sputum on slides for microscopy
(c) intestinal form	Same	Same	Faeces in special sterile tube or in well-closed sterile test-tube Parts of the carcass of the suspicious animal, fur and leather articles manufactured from suspicious raw material (wool and pieces of leather from various parts, in sterile test-tubes) must be sent to laboratories
Tularemia	Next day	From the 8th or 9th day	1. Blood (4-5 ml) in test-tube for agglutination test 2. Carcasses of dead animals as in plague

(Continued)

Disease	Material	Day of the disease	Time of laboratory reply	Note
Plague: (a) bubonic form	1. Blood for haemoculture (10 ml) inoculated in nutrient medium at patient's bedside, then placed in thermostat at 37°C) 2. Specimen of bubo obtained by puncture: smears on slides and inoculation in nutrient medium on location Sputum in special tube and as smears on slides	From the 1st day	In 2-3 days	Strict precautions must be taken. Material must be carefully packed and sealed
		From the 1st day	Same	
		From the 1st day	Smears the same day. Biological test between 7th and 10th days	
(b) pulmonary form			Same	
Smallpox	Contents of vesicles and pustules	Same	In 3-4 days	

Supplement 3

M. A. MOROSOV'S METHOD OF SILVERING FOR VIROSCOPY

As thin as possible a smear of the pathologic substrate to be examined (for example, the contents of a pustule of a smallpox patient) is made on a dry, degreased slide; the smear is dried in the air at room temperature without fixation. Then the smear is covered for 1 minute with Ruge's solution, after which it is washed with distilled water and treated for 2 minutes with reagent No. 2 (see below), while being lightly heated to the point of appearance of weak vapours.

Then, after being thoroughly washed with distilled water, the smear is treated for 2 minutes with reagent No. 3, while being lightly heated until the preparation turns dark-brown, washed again with a stream of distilled water, dried in the air and examined under the microscope with the aid of an immersion system. If the results of microscopy are positive, it is possible to discover a large number of roundish structures (250-300 μ) arranged in the field of vision singly, in chains or in clusters.

Reagent No. 1 (Ruge's solution). 1 ml of glacial acetic acid and 2 ml of formalin dissolved in 100 ml of distilled water.

Reagent No. 2. 5 g of tannin and 1 ml of liquid carbolic acid dissolved in 100 ml of distilled water.

Reagent No. 3. To 80 ml of a 5 per cent aqueous solution of crystalline silver nitrate a 25 per cent ammonia solution is added drop by drop until the yellow-brown and brown-black precipitates which have formed completely dissolve and the liquid becomes slightly opalescent.

Supplement 4

STAINING SMEARS AND THICK DROPS FOR THE PURPOSE OF REVEALING MALARIAL PLASMODIA AND RELAPSING FEVER SPIROCHAETES

Blood smears on slides are prepared and stained by Romanovsky-Giemsa's method in the same manner as the smears for a leucocyte count.

To prepare a thick drop, 2 or 3 thick drops of blood are placed on a slide and smeared over it until the drop is about 18 mm in diameter. Then the resultant thick drop, protected from dust and flies by a loose-fitting Petri dish cover, is dried in the air (without fixation). Thick drops are stained by a working solution of Romanovsky-Giemsa's stain; the slides are placed on parallel glass rods which are, in turn, placed on the sides of a cuvette or bath. The stain solution is applied to the slide by means of a pipette or a rubber bulb.

The working solution of Romanovsky-Giemsa's stain is poured on the slide containing the thick drops of blood and is allowed to stand for 30-45 minutes at room temperature. It is necessary closely to observe D. N. Zasukhin's staining rules (1957) described below.

The best results of staining by Romanovsky-Giemsa's method are produced in weakly-alkaline water with an approximate pH of 6.2-7.1. But, since the main solutions of this stain offered in the market do not always possess uniform properties, it is desirable that an optimum pH value should be chosen for each batch (vial) of the stain. For this purpose 3-4 buffer mixtures are prepared with pH=5.8-6.2-6.8-7.2 or 6.0-6.6-7.2 and the stain being tested is dissolved in them (1-2 drops per 1 ml of mixture). As test material fresh drop smears fixed in methyl alcohol for 3 minutes are used.

Most laboratories in the USSR now use a commercial "Romanovsky azure-cosin" stain. The stain is sold as the basic solution from which the working solution is prepared by its 1 : 10 dilution in distilled water (2 drops of the basic solution in 1 ml of water).

At above-room temperature the staining time may be shortened; at below-room temperature it is, on the contrary, prolonged. The stain is washed off either with a stream of water from the tap or by immersion in a vessel containing water. This must be done carefully because the drop may become disengaged from the slide (the stream of water must be directed at the edge of the slide and not at the drop). After staining, the thick drops are dried on racks and are examined under the immersion objective of a microscope.

It should be remembered that good results of staining smears and thick drops are produced only when the following requisite rules are observed: (a) the water used for diluting the stain is suitable for the purpose (reaction, purity); (b) the stain is of good quality; (c) the slides on which the smears or thick drops are prepared are washed clean; (d) the smears and thick drops are well prepared shortly before use.

In some cases, when the desired stain cannot be produced, alkaline methylene blue (10 drops per 100 ml) may be added to the solution of Romanovsky's stain.

Sometimes Romanovsky's stain is sold dry, in the form of powder or tablets. A working solution is prepared from dry stain as follows: 3.8 g of the dry stain is triturated in a mortar, a small amount of 192 proof ethyl alcohol and glycerin (equal amounts) is added and the mixture continues to be triturated. Then up to 500 ml of alcohol and glycerin (250 ml each) are added. The alcohol and glycerin must be chemically pure. The stain dissolves slowly, over a period of several days. To hasten the solution, the vial with the stain may be placed in a thermostat for 24 hours at 37-60°C. When the stain has dissolved it may be used as the usual commercial solution of the indicated stain. In some cases, when it is necessary to stain the preparations by Romanovsky's method rapidly, the following may be done. An equal amount of pure methyl alcohol is added to the solution of Romanovsky's stain (commercial or prepared from dry stain). The resultant mixture is poured on an unfixed blood smear. The staining period is about 1 minute. Then, without pouring the stain off, distilled water is poured on the smear, the slide (or rack) being moved to-and-fro in order to mix the liquids. After this the staining is continued for another 5-10 minutes. Then the stain is washed off and the smear is dried and examined as usual.

Supplement 5

LIVER FUNCTION TESTS IN BOTKIN'S DISEASE

Normal: bilirubin—0.6 mg% (indirect van den Bergh's test); cholesterol—130-180 mg% (Engelgardt-Smirnova test); prothrombin index—90-100 per cent; thymol test—1-4 units; mercury bichloride test—above 1.8; blood serum albumin fraction—4.5-5.5 per cent; globulin fraction—2-2.5 per cent.

In moderately severe cases of Botkin's disease: blood bilirubin—about 3-4mg% (direct, often rapid and sharp reaction); prothrombin index—70-80 per cent; thymol test—up to 10 units; mercury bichloride test—about 1.5-1.4; gamma-globulin in blood serum—elevated; hypocholesteremia.

In severe cases of Botkin's disease: bilirubin—above 4 mg% (direct, rapid, sharp reaction); prothrombin index—below 70 per cent; thymol test—up to 15-25 units; mercury bichloride test—about 1.3-0.9; gamma-globulin in blood serum considerably elevated; clearly marked hypocholesteremia. Vicisol test is disturbed; intramuscular administration of 0.3 per cent vicisol to healthy people causes rise in prothrombin index within 24 hours, whereas in severe cases of Botkin's disease no such rise is observed.

Supplement 6

RULES GOVERNING DISCHARGE OF CONVALESCENTS FROM HOSPITAL AFTER TREATMENT WITH DRUGS AND ANTIBIOTICS

The principal rule governing the discharge of persons recovering from acute infectious diseases from hospital is adequate clinical cure. This rule also applies to persons treated with drugs and antibiotics. However, since convalescents from infectious diseases may continue to be contagious even when the clinical signs of the disease have disappeared, it is necessary to adhere to certain schedules of isolation envisaged in the special instructions of the USSR Ministry of Health.

Some infectious diseases additionally require microbiological control for the purpose of revealing infection carriers and taking appropriate anti epidemic measures. The rules governing the discharge of convalescents from hospitals after specific treatment are given below. The general rule—adequate clinical cure—remains in effect in all cases.

Amoebiasis. After discharge from hospital persons working in the food industry, grocery stores, canteens, milk kitchens, kindergartens, nurseries and the water-supply system (all conditionally referred to as "food workers") must be kept under medical observation by the district physician and epidemiologist. A check-up for dysentery amoeba-carrying must be periodically made for the purpose of revealing tissue forms of hystolytic amoebae in the faeces. Food workers discovered to carry pathogenic amoebae must be given two courses of treatment with yutren (as outpatients, while continuing to work).

Typhoid fever and paratyphoids A and B. Convalescents may not be discharged from hospital before the 23rd day following complete normalization of temperature (persons treated with synthomycin and levomycetin).

Inoculations of the convalescents' faeces and urine should be made on the 14th, 16th and 18th days of normal temperature; an additional inoculation of the bile obtained by duodenal sounding should be made on the 16th day of normal temperature.

For the purpose of revealing chronic bacteria carriers control bacteriological tests of the convalescents' faeces and urine must be made every 3-4 months and a bile culture once over a period of 2 years after their discharge from hospital. Food workers who have recovered from an attack of typhoid fever must not be allowed to work for 1 month after discharge from hospital. Subsequently their faeces and urine must be subjected to bacteriological tests during the following periods: five times during the first month, then monthly during the first year (if the first five tests proved negative and the food worker was allowed to go back to work). During the subsequent 5 years the faeces and urine of these persons must be subjected to bacteriological tests every 3 months. If even one of the tests proves positive, the subsequent tests must be carried out as during the first month following the discharge from hospital.

Dysentery. Convalescents may be discharged after disappearance of the clinical symptoms, but not before the 7th day of the disease; in cases of earlier discharge from hospital dysentery patients must be treated as outpatients and must be kept under observation by the intestinal contagious department of the hospital or polyclinic. In cases of early discharge from hospital (on the 7th or 8th day of the disease) it is necessary to consider the epidemiological situation in which the convalescents will find themselves after their discharge. Food workers must additionally show negative results of three inoculations of their faeces made in Ploskiryov's medium at 2-day intervals.

Cholera. In addition to clinical cure persons discharged from isolators must show negative results of two inoculations of their faeces in alkalized 1 per cent peptone water and in alkaline agar in Petri dishes.

The first inoculation must not be made before the 6th day of the disease; the subsequent inoculations must be made at intervals of two days.

Relapsing fever. Convalescents must not be discharged before the 23rd day following the end of the last attack.

Visceral leishmaniasis (see treatment of visceral leishmaniasis with solusurmino).

Typhus. In cases of adequate clinical cure convalescents must not be discharged before the 12th day of apyrexia.

Diphtheria. In addition to the disappearance of the clinical symptoms negative results of two bacteriological tests of the mucus taken separately from the fauces and nose (for the purpose of revealing Loeffler's bacteria) are required for the discharge of convalescents from hospital. Bacteria carriers are dealt with in accordance with special instructions.

Epidemic cerebrospinal meningitis. Convalescents may be discharged after disappearance of the clinical symptoms, sufficient normalization of the cerebro-

spinal fluid and negative results of two bacteriological tests of the mucus for meningococci (mucus taken from the nasopharynx), but not before the 30th day of the disease.

Anthrax. Patients with the cutaneous form of anthrax must be isolated until disengagement of the scab, cicatrization and complete epithelization of the ulcer. Patients with pulmonary form of the disease may be discharged after disappearance of the clinical symptoms and negative results of two bacteriological tests of the sputum made at a 5-day interval.

Plague. Patients surviving bubonic plague may not be discharged earlier than 1 month after disappearance of all clinical symptoms and negative results of two bacteriological tests of specimens obtained by puncturing the buboes at a 2-day interval.

In cases of primary pulmonary plague and metastatic pneumonic plague patients may be discharged only after complete clinical cure and negative results of numerous bacteriological tests of the sputum. All persons who have had any contact with plague patients must be given preventive treatment with streptomycin (1-1.5 g per day for 5 days).

Supplement 7

PRESCRIPTIONS

1. Antibiotics

- Rp. Albomycini 1,000,000 U**
D.t.d. N. 24 in amp.
S. Dissolve contents of
5 ampules in 10 ml of
twice-distilled water
before administration
and inject this dose sub-
cutaneously twice a day
- Rp. Biomycini hydrochlorici**
100,000 U
D.t.d. N. 60
S. 2 pills 4 times per day
- Rp. Laovomycotini 0.5**
D.t.d. N. 40
S. 1 pill 6 times per day
- Rp. Novocillini 5.0**
D.t.d. N. 6 in amp.
S. For intramuscular admin-
istration of 2 ml twice a day

- Rp. Penicillini crystallisati 300,000 U**
D.t.d. N. 12
S. For intramuscular administration of 300,000 U twice a day; the dose must be dissolved in 2 ml of a 0.5 per cent novocain or ecmolin solution
- Rp. Sol. Novocaini 0.25% 2.0**
D.t.d. N. 6 in amp.
S. For dissolving penicillin before administration
- Rp. Bicillini 3,600,000 U**
DS. For intramuscular administration
- Rp. Novocillini 5.0**
D.t.d. N. 10 in amp.
For intramuscular injections of 1 ampule twice a day
- Rp. Penicillini-natrio crystallisati pro injectionibus 100,000 U**
Aq. bidestill. sterilis. 2.0
MDS. For endolumbar administration of 100,000 U once a day
- Rp. Streptomycini hydrochlorici 500,000 U**
D.t.d. N. 6
S. Dissolve contents of vial in 2 ml of twice-distilled water and administer intramuscularly 1 ml of the solution twice a day
- Rp. Synthomycini 0.5**
D.t.d. in tabul. N. 40
S. 1 pill 6 times per day
- Rp. Tetracyclini 0.3**
D.t.d. N. 24 in caps. gelat.
S. 1 capsule 4 times per day, drinking it down with plenty of water
- Rp. Terramycini 0.1**
D.t.d. N. 80 in tabul.
S. 4 pills per intake 4 times per day

2. Drugs

- Rp. Streptocidi albi 0.5**
D.t.d N. 25 in tabul.
S. 1 pill 5 times per day
- Rp. Phthalazoli 0.5**
D.t.d. N. 40
S. 2 pills 4 times per day
- Rp. Norsulfazoli 0.5**
D.t.d. N. 20 in tabul.
S. 2 pills 5 times per day
- Rp. Sol. Norsulfazoli 20% 25.0**
Sterilisetur!
DS. For intravenous infusions
5 ml twice a day
- Rp. Sol. Aethazoli-natrii 20% 10.0**
D.t.d. N. 12 in amp.
S. 1 ampule intravenously
twice a day
- Rp. Disulformini 0.5**
D.t.d. N. 30
S. 2 pills 6 times per day,
none at night
- Rp. Novarsenoli 0.45**
D.t.d. N. 10
S. Contents of ampule to be
dissolved in 5 ml of twice-
distilled sterile water imme-
diately before intravenous in-
fusion; to be administered
slowly
- Rp. Aminarsoni 0.25**
D.t.d. N. 20 in tabul.
S. 1 pill 3 times per day
(for adults) for 10 days
- Rp. Sol. Emetini hydrochlorici 2% 20.0**
Sterilisetur!
DS. 1.5 ml intramuscularly twice a day

Rp. Yatreni 0.5
D.t.d. N. 10 in caps. gelatinosis
S. 1 capsule (for adults) twice a day

Rp. Sol. Solusurmini 20% 60.0
Steriliseturi
DS. To be administered intramuscularly
according to a special scheme

3. Serums, Therapeutic Vaccines, Diagnostic Biologic Preparations, Bacteriophage

Antitetanic serum (tetanus antitoxin)—100,000-200,000 U intramuscularly once a day.

"Diaferm" antidiphtheritic antitoxic serum—10,000-30,000 U intramuscularly once a day.

Antibotulinus serum—60,000-150,000 U intramuscularly twice a day.

Antianthrax (antibacterial) serum—50-60 ml intramuscularly once a day.

Antimeasles serum—30 ml for a single intramuscular administration to 3-4-year-old children.

Gamma-globulin—3 ml (in ampule) for a single intramuscular administration to 3-year-old children.

Rp. Seri antibiotulinici 50,000 U
D.t.d. N. 12 in amp.
S. 100,000 U subcutaneously
twice a day

Rp. Seri antidiphtherici 10,000 U
D.t.d. in amp.
S. 10,000 U intramuscularly
twice a day

Rp. Seri antidyenterici 10,000 U
D.t.d. N. 6 in amp.
**S. Single intramuscular admin-
 istration of 6 ampules**

Rp. Seri antitetanici 25,000 U
D.t.d. N. 6 in amp.
S. Intramuscular administration
of all 6 ampules

Therapeutic brucella vaccine in 1-ml ampules—to be administered intramuscularly, diluted in physiologic solution to yield requisite number of microbial bodies (in accordance with the scheme of treatment).

Chernokhvostov's dysentery (Flexner-Sonne) alcohol vaccine in 1-ml ampules—to be administered subcutaneously in accordance with the scheme of treatment.

Therapeutic tularaemia vaccine in 1-ml ampules—to be administered subcutaneously in accordance with the scheme of treatment.

Brucellin 1 ml (in ampule)—0.1 ml to be administered intracutaneously into the forearm for Burnet's allergic test.

Tularin 1 ml (in ampule)—0.1 ml to be administered intracutaneously into the forearm for allergic diagnosis of tularaemia.

Cholera bacteriophage 50 ml—to be taken twice a day in a dose of 25 ml 2 hours before meals and followed by drinking 1 glassful of warm boiled water.

4. Antimalarial Agents

Rp. Acrichini 0.1
D.t.d. N. 25
S. 1 pill 3 times per day
(according to the scheme of treatment)

Rp. Sol. Acrichini hydrochlorici pro injectionibus 4% 30.0
DS. For intramuscular injections in a dose of 8 ml twice a day

Rp. Bigumali 0.1
D.t.d. N. 24 in tabul.
S. 1 pill 3 times per day
(according to the scheme of treatment)

Rp. Plasmocidi 0.02
Acrichini hydrochlorici 0.1
D.t.d. N. 30 in tabul.
S. 1 pill 3 times per day

Rp. Plasmocidi 0.02
Sacchari 0.15
M. f. pulv.
D.t.d. N. 10
S. 1 powder 3 times per day

Rp. Chinini hydrochlorici 0.5
D.t.d. N. 12
S. 1 powder 3 times a day

Rp. Chinini bihydrochlorici 5.0
Aq. bidestill. ad 10.0
Sterilliseturi
MDS. 2 ml intramuscularly
once a day

Rp. Chinocidi 0.01
D.t.d. N. 30 in tabul.
S. 1 pill twice a day

5. Anthelmintics

- Rp. Santonini 0.1**
Sacchari albi 0.15
M. f. pulv.
D.t.d. N. 6
S. 1 powder 3 times per day
(in the morning on an empty
stomach for 2 days) at 1-hour
intervals (for adults)
- Rp. Tabul. Saccapheni**
D.t.d. N. 20
S. 10 pills per day to be
taken in the morning on an
empty stomach in the course of
one hour (2-day course of
treatment)
- Rp. Extr. Filicis maris aetherei 0.5**
D.t.d. N. 10 in caps. gelatinosis
S. The entire dose to be taken on an
empty stomach at the rate of 1 capsule
every 3 minutes (in cases of taeniasis)
- Rp. Sulfuris de purati 0.5**
D.t.d. N. 30
S. 2 powders 3 times per day
before meals for 5 days running
(for adults)
- Rp. Heptylresorcini 0.1**
D.t.d. N. 15 in tabul.
S. 15 pills to be taken on an
empty stomach at the rate of
1 pill every 5 minutes on the
day of treatment (for adults)
- Rp. Osarsoli 0.25**
D.t.d. N. 10
S. 1 pill (in accordance with the
scheme of treatment)
- Rp. Piperasini adipinici 0.25**
D.t.d. N. 10
S. 4 pills twice a day
after meals (for 12-year-olds)

G. Spasmolytics, Analgesics and Hypnotics

- Rp. Chlorali hydrati 1.0**
Aq. destill.
Mucilag. amylii an 25.0
MDS. For one enema (in cases of
convulsions in tetanus patients)
- Rp. Morphini hydrochlorici 1% 1.0**
D.t.d. N. 6 in amp.
S. 1 ml subcutaneously
(on indications)
- Rp. Sol. Pantoponi 2% 1.0**
D.t.d. N. 6 in amp.
S. 1 ml subcutaneously
(on indications)
- Rp. Promedoli 0.025**
Sacchari albi 0.15
M. f. pulv.
D.t.d. N. 6
S. 1 powder twice a day
- Rp. Dibazoli 0.005**
Sacchari albi 0.2
M.f. pulv.
D.t.d. N. 20
S. 1 powder twice a day
- Rp. Sol. Proserini 0.05% 20.0**
Steriliseturf
DS. To be administered subcutaneously
by special prescription of a physician
- Rp. Analgini 0.5**
D.t.d. N. 10
S. 1 pill 2-3 times per day
- Rp. Barbamyli 0.2**
D.t.d. N. 6
S. 1. powder before sleep
- Rp. Medinali 0.5**
D.t.d. N. 6 in tabul.
S. 1 pill 1 hour before sleep
drunk down with warm water

7. Vitamins and Haemostatics

- Rp. Sol. Thiamini-bromati 1.2% 1.0**
D.t.d. N. 15 in amp.
S. For intramuscular injections
in a dose of 1 ml twice a day
- Rp. Vitamini B₁₂ in amp. 0.0001**
D.t.d. N. 20
S. 1 ampule intramuscularly
twice a day
- Rp. Sol. Acidi ascorbinici 5% 1.0**
D.t.d. N. 20 in amp.
S. To be administered intravenously
in a dose of 2 ampules once a day.
dissolving the contents of the ampules
in 40 ml of a 40% glucose solution
- Rp. Vicasoli 0.015**
D.t.d. N. 10 in tabul.
S. 1 pill twice a day for 4 days
- Rp. Vitamini P 0.015**
Acidi ascorbinici 0.15
M.f. pulv.
D.t.d. N. 20
S. 1 powder 3 times per day
- Rp. Sol. Calcii chlorati 10% 10.0**
D.t.d. N. 6 in amp.
S. 10 ml intravenously
twice a day

8. Cardiovascular Stimulants

- Rp. Cordiamini 2.0**
D.t.d. N. 6. in amp.
S. 1 ampule subcutaneously
3 times per day
- Rp. Cordiamini 10.0**
DS. 20-25 drops
3 times per day
- Rp. Sol. Ephedrini hydrochlorici 5% 1.0**
D.t.d. N. 6 in amp.
S. 0.6-1 ml subcutaneously
or intramuscularly 3 times per day

Rp. Ephedrini hydrochlorici 0.025
Sacchari 0.15
M.f. pulv.
D.t.d. N. 12
S. 1 powder 3 times per day

Rp. Sol. Corazoli 10% 1.0
D.t.d. N. 6 in amp.
S. 1 ml subcutaneously
3 times per day

Rp. Sol. Corgliconi 0.06% 1.0
D.t.d. in amp. N. 10
S. 0.5-1 ml intravenously
together with 20 ml of a
40% glucose solution; to be
administered slowly

Rp. Ol. Camphorae 20% 1.0
D.t.d. N. 20 in amp.
S. 2 ampules subcutaneously
3 times per day

Rp. Sol. Strychnini nitrici 0.1% 1.0
D.t.d. N. 6 in amp.
S. 1 ml subcutaneously
3 times per day

Rp. Cytitoni 1.0
D.t.d. N. 6 in amp.
S. 1 ml intravenously (for adults),
to be administered slowly

Rp. Sol. Strophanthini 0.05% 1.0
D.t.d. N. 3 in amp.
S. 0.25-0.5 ml intravenously
(to be dissolved before adminis-
tration in 10 ml of a 40% glucose
solution and administered over a
period of 3 minutes)

Rp. Sol. Mesatoni 1% 1.0
D.t.d. N. 6 in amp.
S. 0.6 ml intramuscularly

9. Pathogenetic Drugs

Rp. Sol. Diplocini 2% 5.0
D.t.d. N. 6 in amp.
S. For intravenous infusion
according to a special scheme

Rp. Acidi glutaminici 1.0

D.t.d. N. 40

S. 1 powder twice a day

Rp. Prednisoni 0.005

D.t.d. N. 30 in tabul.

S. 1 pill 5 times per day

Rp. Prednisoloni 0.005

D.t.d. N. 30 in tabul.

S. 1 pill 5 times per day

TO THE READER

*Mr Publishers would be glad to have your
opinion on the translation and the design of this book.
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